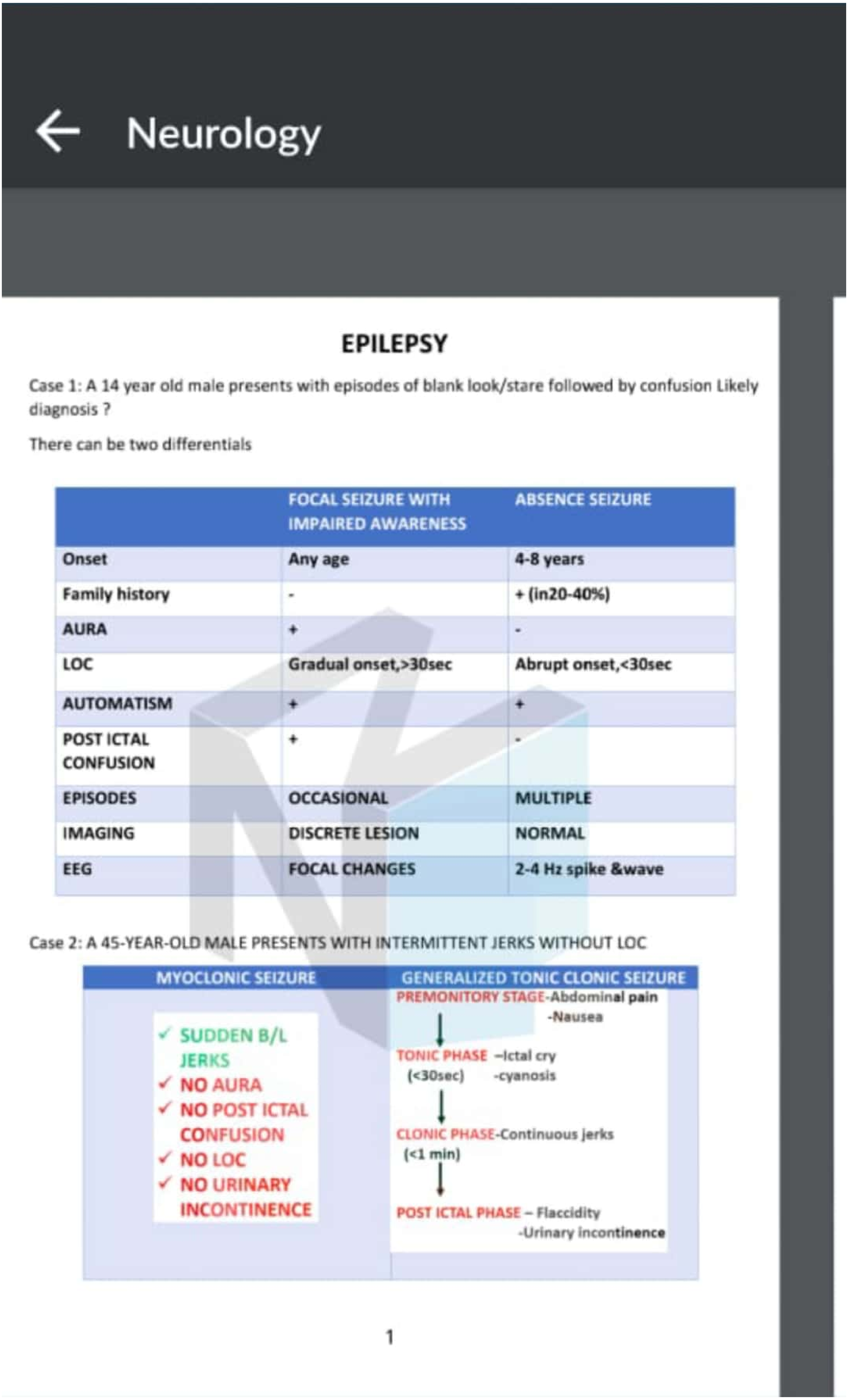


EPILEPSY

Case 1: A 14 year old male presents with episodes of blank look/stare followed by confusion Likely diagnosis ?

There can be two differentials

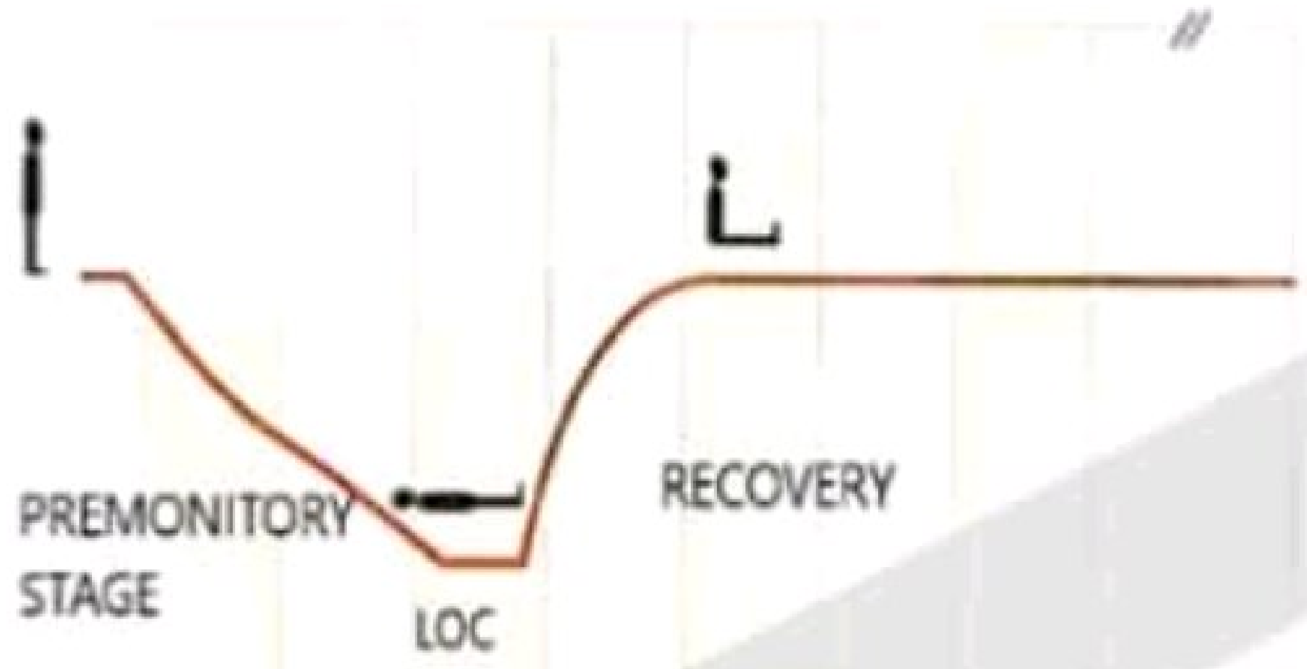
	FOCAL SEIZURE WITH IMPAIRED AWARENESS	ABSENCE SEIZURE
Onset	Any age	4-8 years
Family history	-	+ (in20-40%)
AURA	+	-
LOC	Gradual onset,>30sec	Abrupt onset,<30sec
AUTOMATISM	+	+
POST ICTAL CONFUSION	+	-
EPISODES	OCCASIONAL	MULTIPLE
IMAGING	DISCRETE LESION	NORMAL
EEG	FOCAL CHANGES	2-4 Hz spike &wave

Case 2: A 45-YEAR-OLD MALE PRESENTS WITH INTERMITTENT JERKS WITHOUT LOC

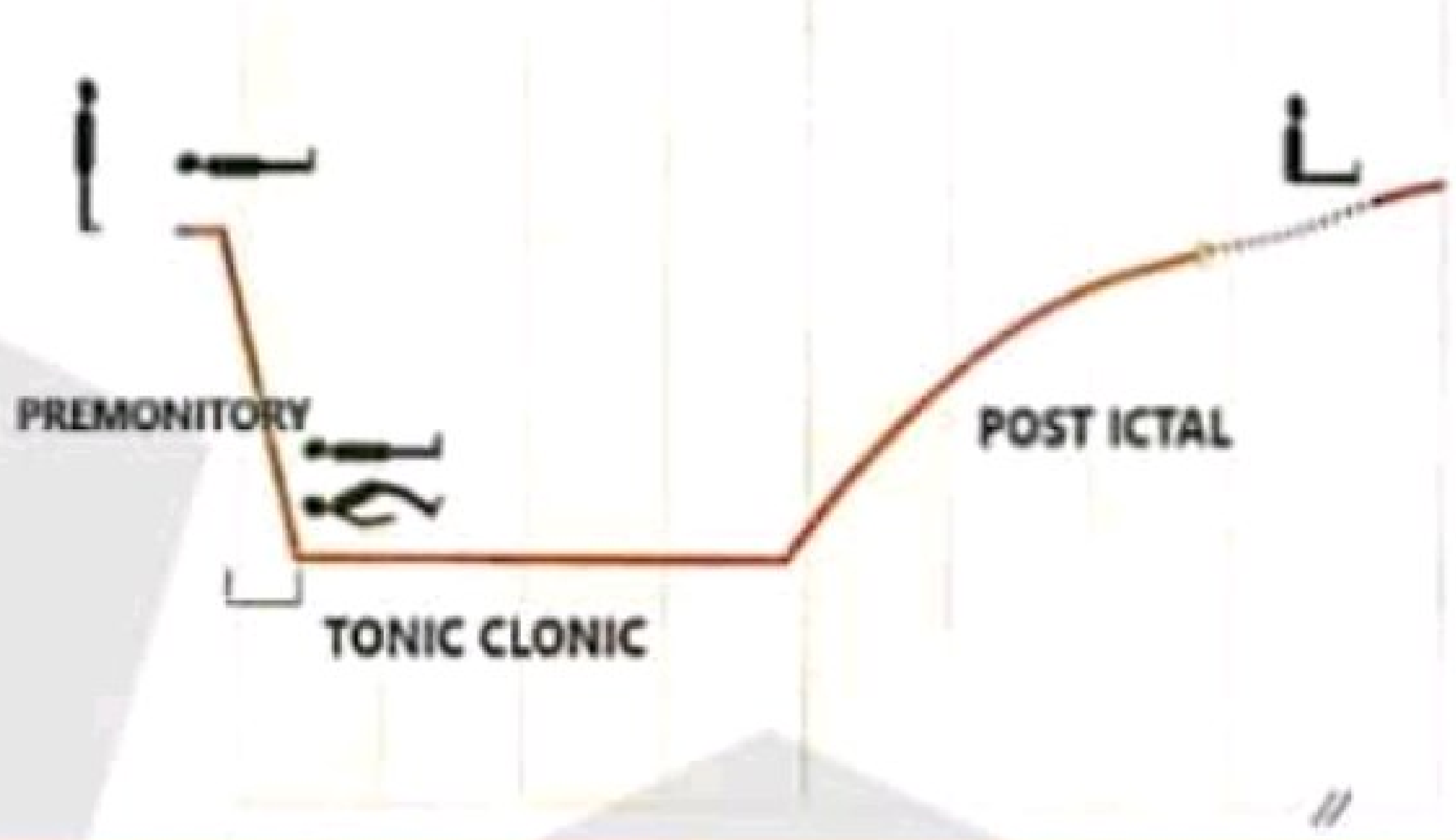
MYOCLONIC SEIZURE	GENERALIZED TONIC CLONIC SEIZURE
✓ SUDDEN B/L JERKS ✓ NO AURA ✓ NO POST ICTAL CONFUSION ✓ NO LOC ✓ NO URINARY INCONTINENCE	PREMONITORY STAGE-Abdominal pain -Nausea ↓ TONIC PHASE –Ictal cry (<30sec) -cyanosis ↓ CLONIC PHASE-Continuous jerks (<1 min) ↓ POST ICTAL PHASE – Flaccidity -Urinary incontinence

Case 2: A 17-year-old girl arrived at class immediately **after cross-country running practice**. While sitting at her desk, **she felt sweaty, warm all over, and nauseated**. She then slumped forward with **fast, jerklike movements of her arms and legs**. Her teacher rushed over to **lower her to the floor, and she quickly began to rouse.** She initially appeared **confused** but was able to answer questions appropriately. She had some **urinary incontinence** during the episode but no tongue trauma. She **returned to her baseline** mental status **within a few minutes** of the episode.

SYNCOPE



SEIZURE



FEATURE	Seizure	Syncope
Immediate precipitating factors	Usually none	Emotional stress, Valsalva, cardiac/autonomic Etiology
Premonitory symptoms	None	Tiredness, nausea, diaphoresis
Posture at onset	Variable	Erect
Transition to unconsciousness	Often Immediate	Gradual over seconds
Duration of LOC	Minutes	Seconds
Duration of tonic clonic movements	30-60 sec	<15 seconds
Facial appearance during event	Cyanosis	Pallor
Disorientation after event	Many minutes-hours	<5 minutes
Aching of muscles after event	Often	Sometimes
Tongue Bite	++ (Lateral margin)	+ (Tip)
Urinary incontinence	+	+
Fecal incontinence	Present	Rare
Headache	+	Rare

Case 3: A patient is confused and displays episodes such as **grimacing, squirming, and flailing of the limbs**; side-to – side movement of the head; and resistance and even thrashing at anyone attempting to assist him. The patient displays **no aura**, and the **EEG** during this period appears approximately **normal** . Which of the following best characterizes this disorder?

a). Generalized seizure

b). Absence seizure

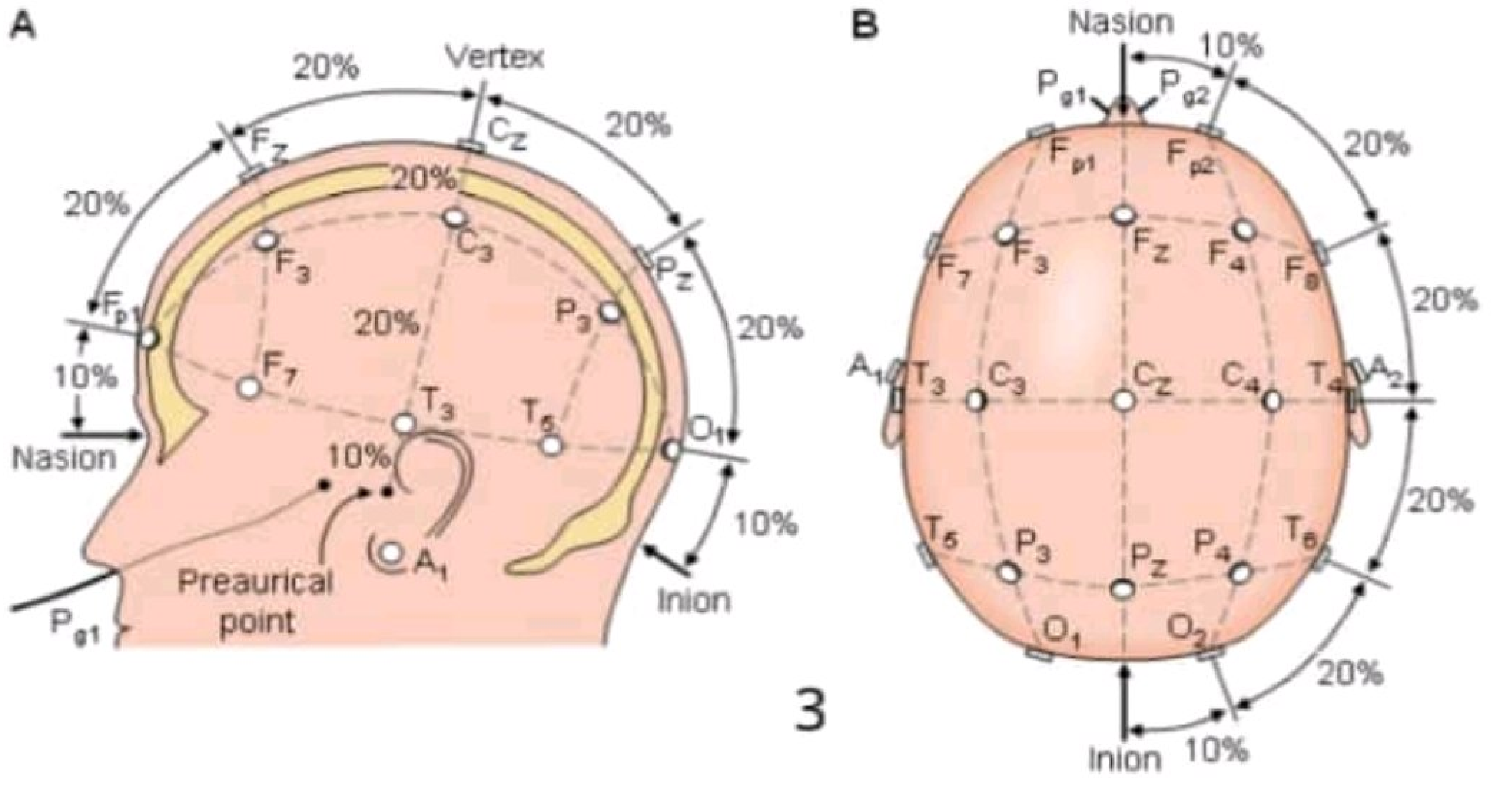
c). Complex partial seizure

d). **Psychogenic seizure (a/k/a PSUEDO-SEIZUERE, Dissociative Convulsions, Hysteria, Functional Neurological Symptoms disorder)**

Best Investigation to differentiate between Seizure and Pseudo-seizure is CLINICAL EXAMINATION and not EEG. (Harrison Update: Best is Video EEG)

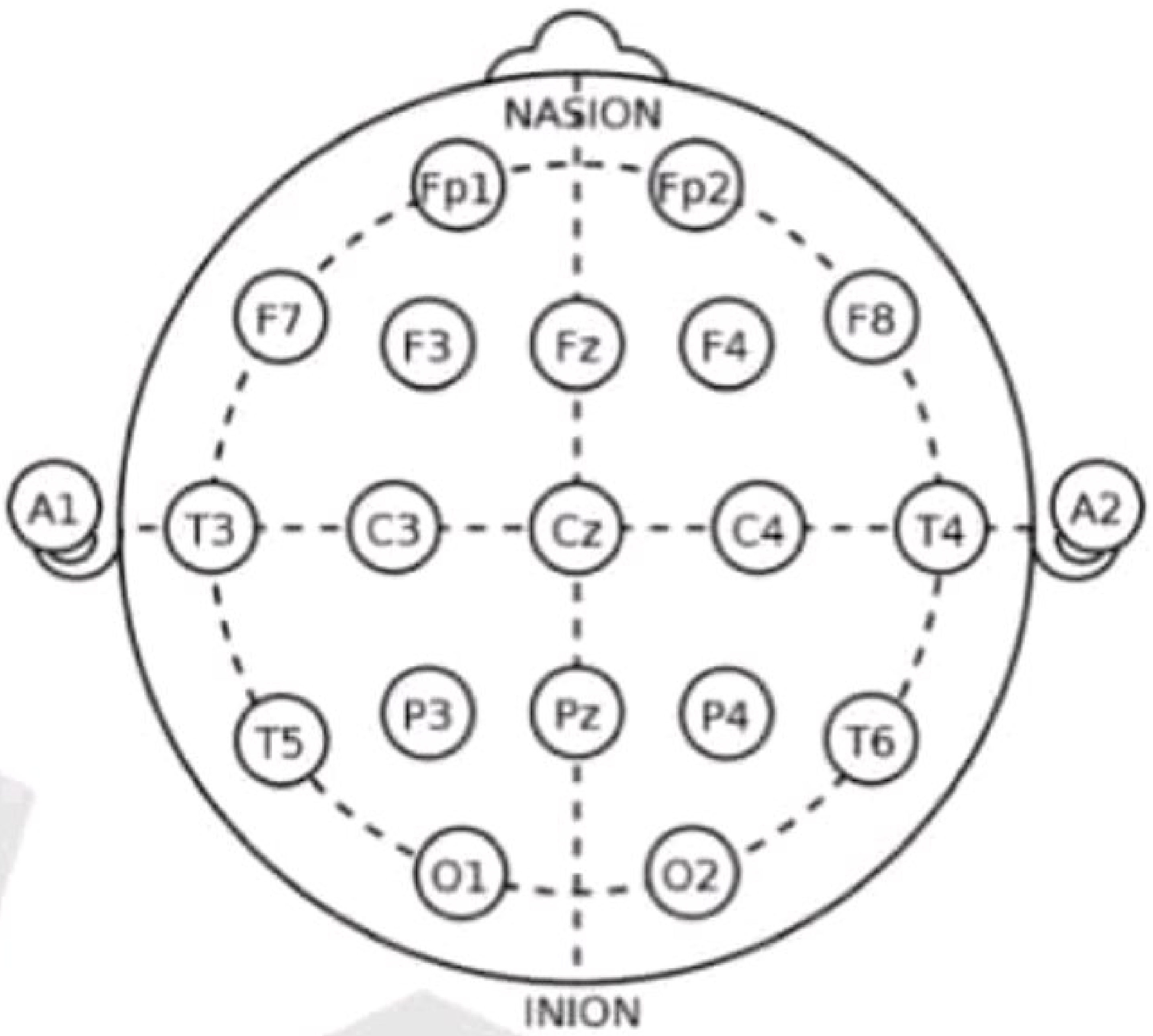
Clinical features	Epileptic S	Dissociative convulsion
Attack pattern	Stereotyped	Absence of any established pattern.
Place of occurrence	anywhere	Usually indoors or at safe place
Warning	Aura is present	variable
Time of the day	Anytime , can occur during sleep	Never occur in sleep
Tongue bite	Usually present	Absent
Incontinence of urine & feces	Can occur	Very rare
Injury	Can occur	Very rare
Speech	No verbalization during seizure	Verbalization may occur
Duration	Usually about 30-70 sec (short)	20-800 sec (Prolonged)
Head turning	Unilateral	Side to side turning
Amnesia	Complete	Partial
Post- ictal confusion	Present	Absent
EEG	Abnormal	Normal
Serum Prolactin	Increased in post- ictal period	Usually Normal

EEG


A
20%
Vertex
Fz
Cz
20%
20%
20%
F3
C3
Pz
Fp1
20%
P3
20%
10%
F7
T3
T5
O1
Nasion
10%
10%
Preauricular point
A1
Inion
Pg1
B
Nasion
10%
Pg1
Pg2
Fp1
Fp2
20%
F7
F3
Fz
F4
F8
20%
A1
T3
C3
Cz
C4
T4
A2
20%
T5
P3
Pz
P4
T6
O1
O2
20%
Inion
10%

Electrode placement according to **10-20 system**

- Each electrode placement site has a letter to identify the lobe, or area of the brain it is reading from: pre-rontal (Fp), frontal (F), temporal (T), parietal (P), occipital (O), and central (C). Note that there is no "central lobe"; due to their placement, and depending on the individual, the "C" electrodes can exhibit/represent EEG activity more typical of frontal, temporal, and some parietal-occipital activity, and are always utilized in polysomnography sleep studies for the purpose of determining stages of sleep.
- Even-numbered electrodes (2,4,6,8) refer to electrode placement on the right side of the head, whereas odd numbers (1,3,5,7) refer to those on the left



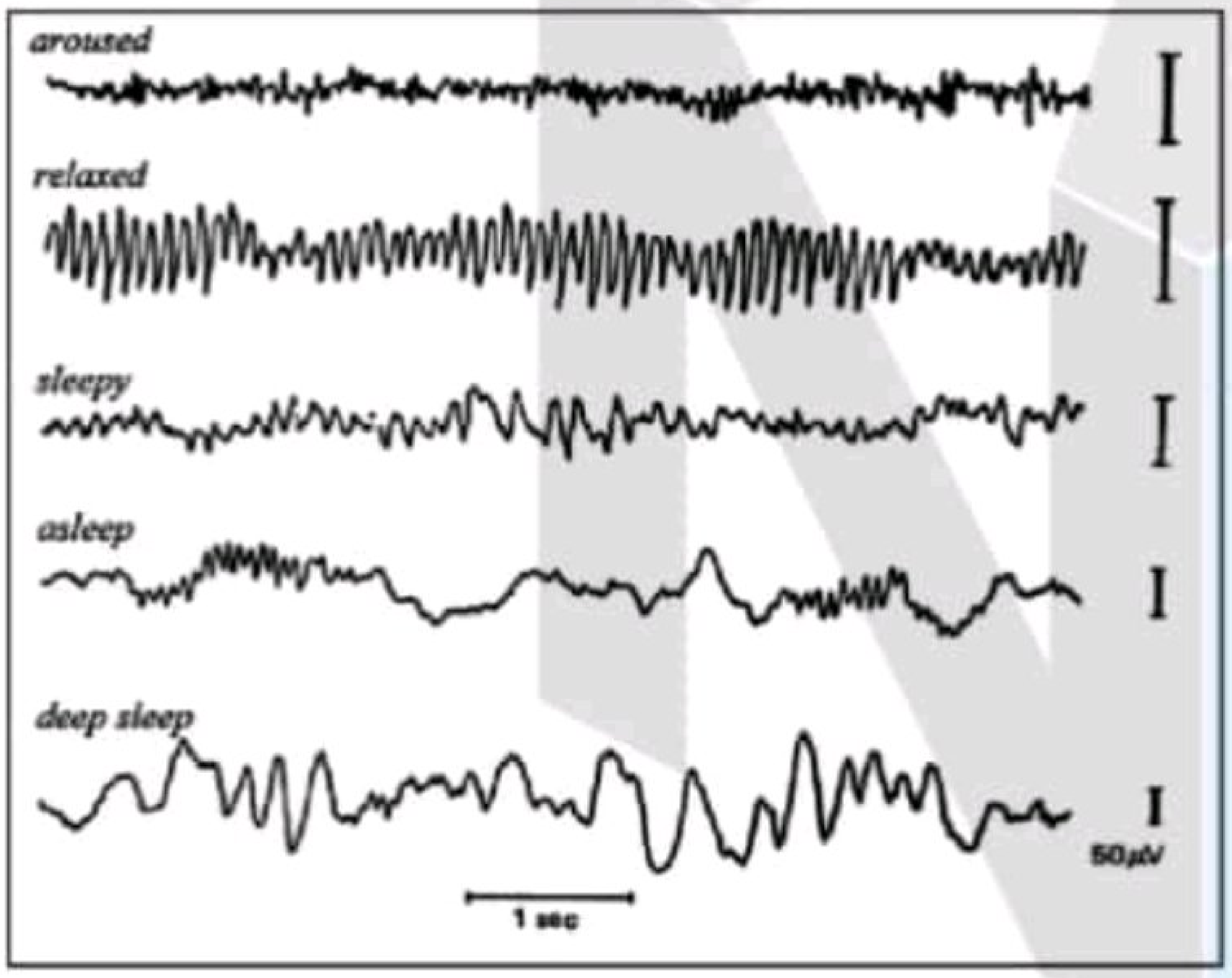
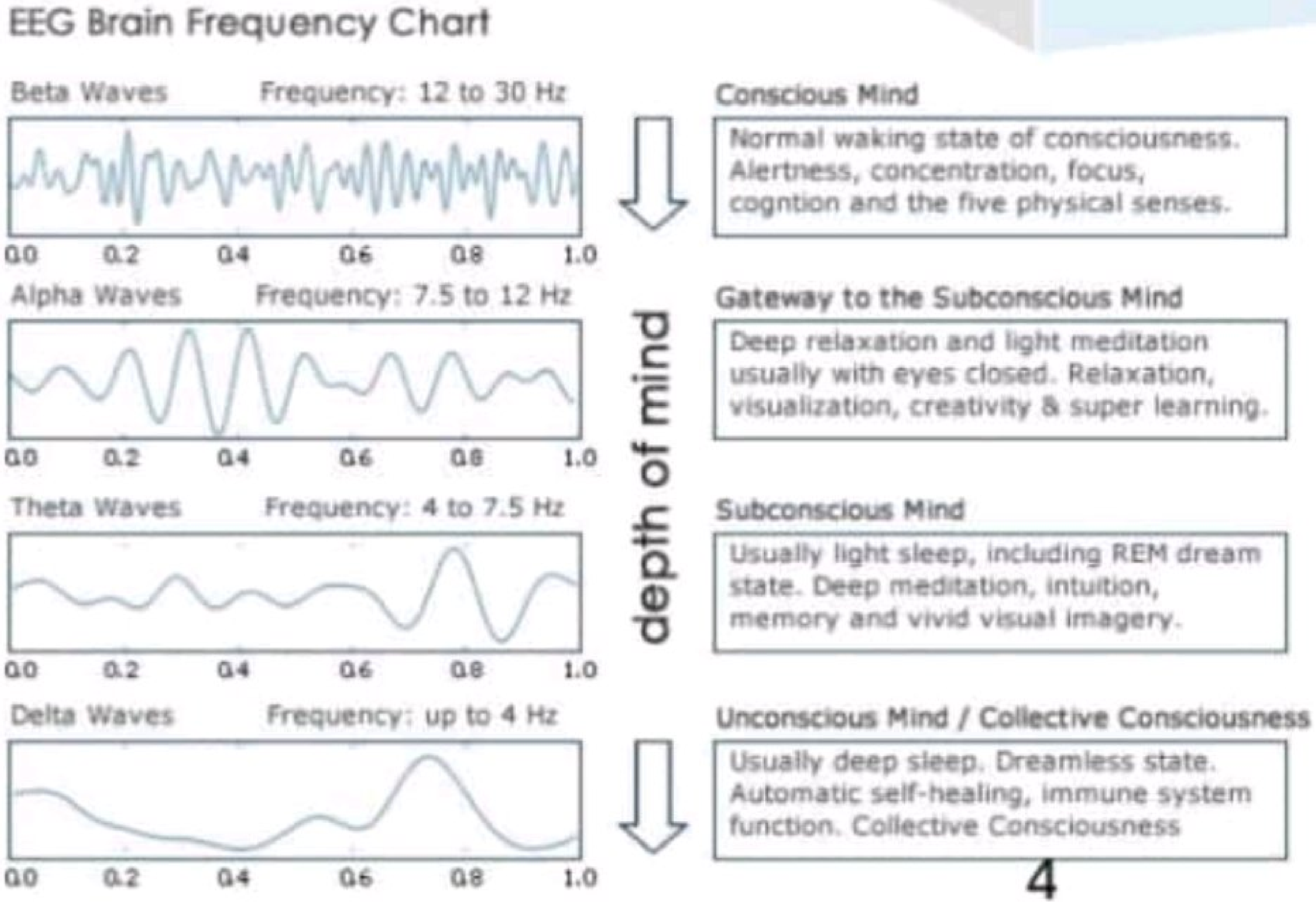


Chart of Background EEG activity



Conscious Mind

Normal waking state of consciousness. Alertness, concentration, focus, cogntion and the five physical senses.

Gateway to the Subconscious Mind

Deep relaxation and light meditation usually with eyes closed. Relaxation, visualization, creativity & super learning.

Subconscious Mind

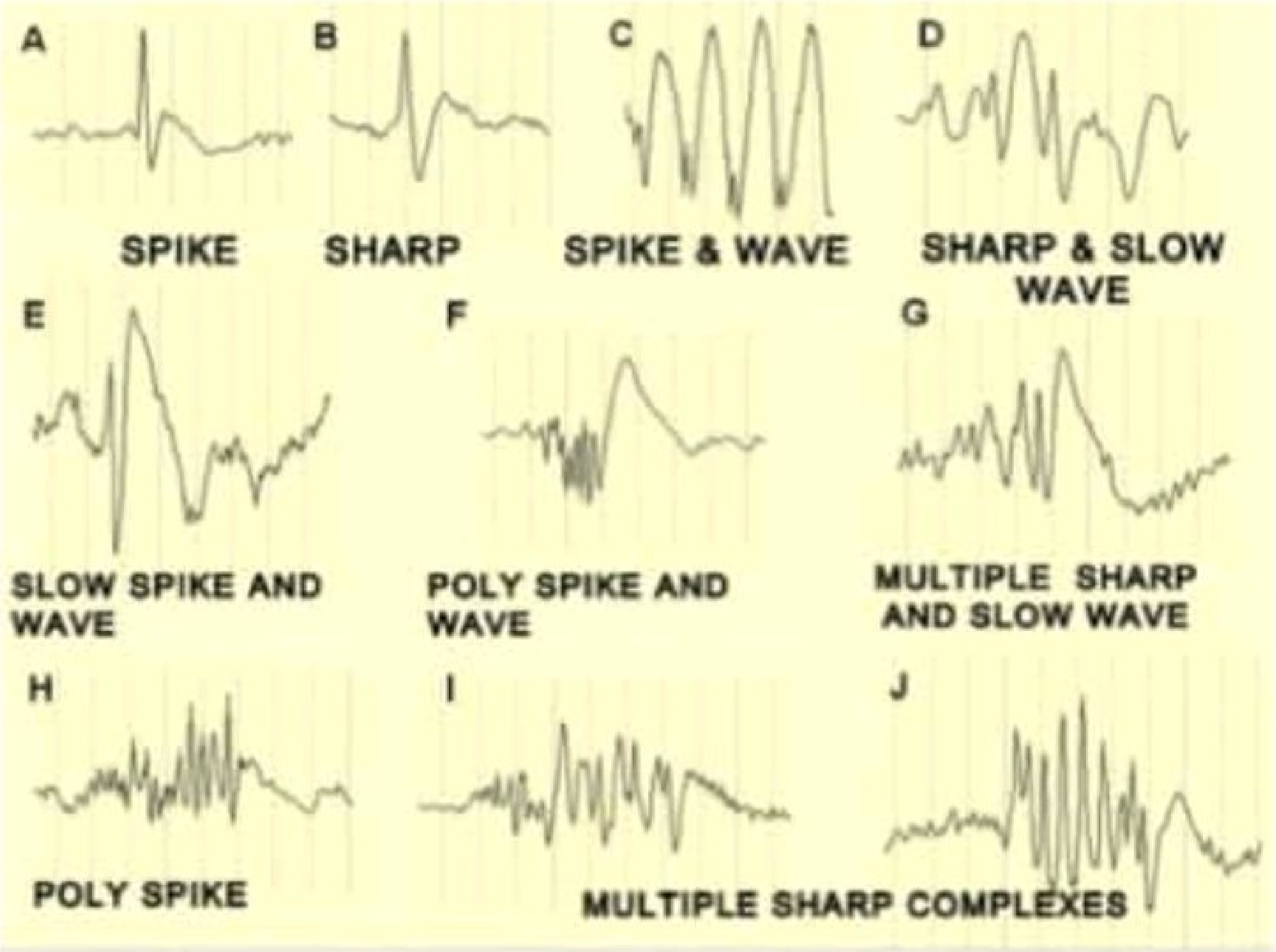
Usually light sleep, including REM dream state. Deep meditation, intuition, memory and vivid visual imagery.

Unconscious Mind / Collective Consciousness

Usually deep sleep. Dreamless state. Automatic self-healing, immune system function. Collective Consciousness

Alpha waves are best recorded in Occipital lobe

ABNORMAL EEG WAVES


A
B
C
D
SPIKE
SHARP
SPIKE & WAVE
SHARP & SLOW WAVE
E
F
G
SLOW SPIKE AND WAVE
POLY SPIKE AND WAVE
MULTIPLE SHARP AND SLOW WAVE
H
I
J
POLY SPIKE
MULTIPLE SHARP COMPLEXES

- Spike : < 70 ms
- Sharp waves : 70 - 200 ms
- Slow waves : > 200 ms

- **If wave finishes before 1/3rd of one 200msec slot → Spike**
- **If wave finishes just at the end of a 200msec slot→ Sharp wave**
- **If >1 slot→ slow wave**

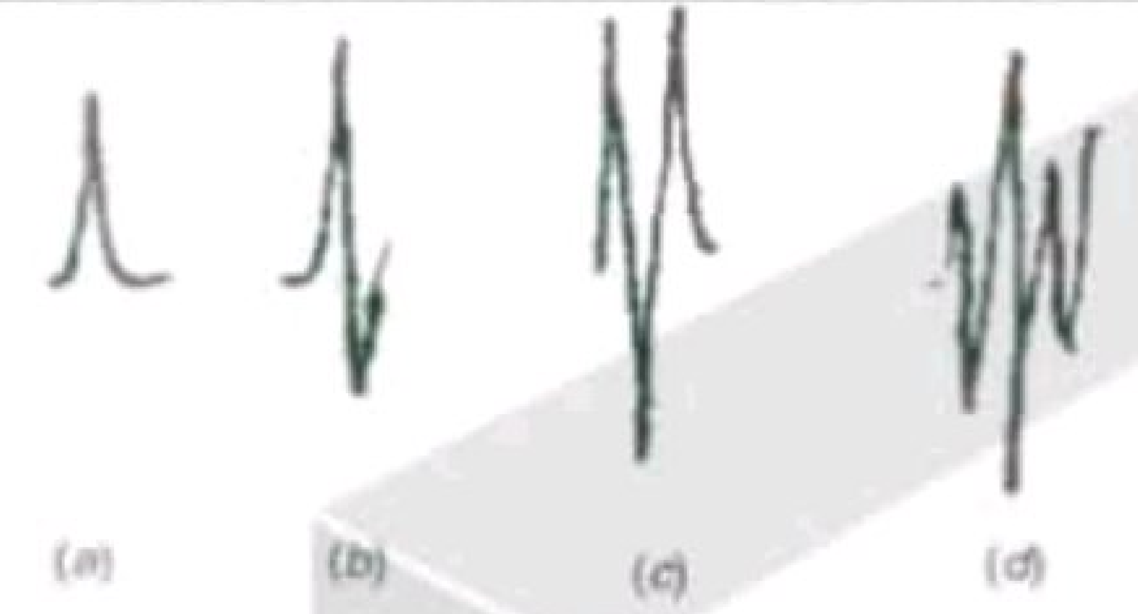


Fig. 5.1 *Schematic diagram showing morphology of spike. It ascends and descends sharply. (a) monophasic, (b) biphasic, (c) triphasic and (d) polyphasic.*

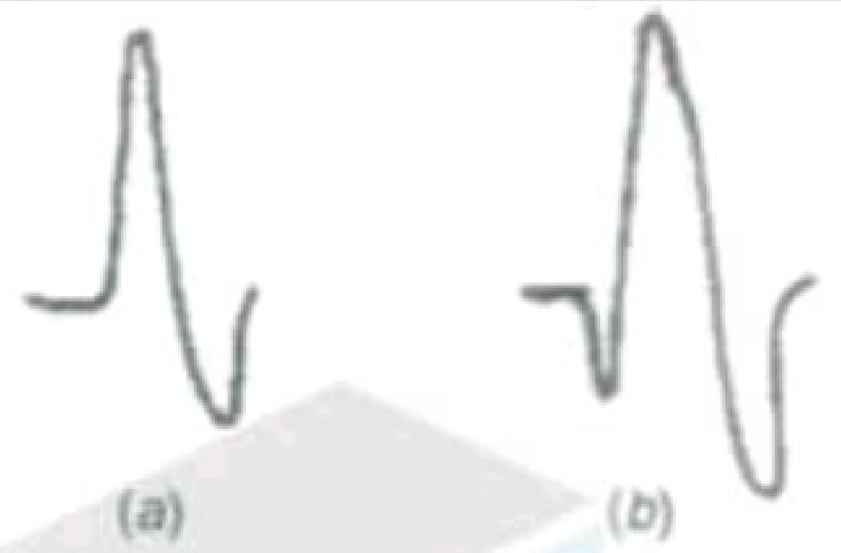
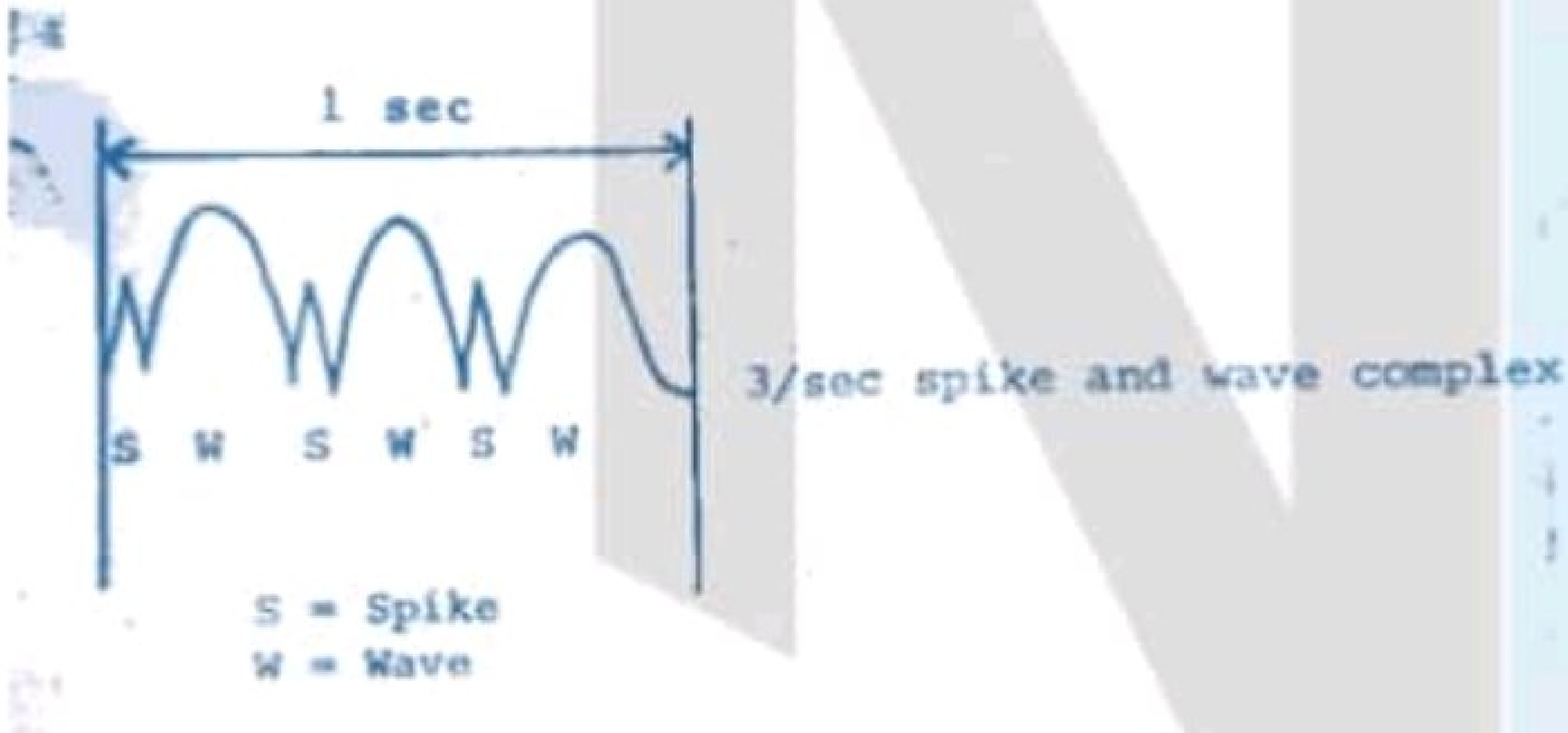


Fig. 5.5 *Schematic diagram showing morphology of sharp waves. It ascends sharply but descends slowly. (a) biphasic and (b) triphasic.*


1 sec
S W S W S W
3/sec spike and wave complex
S = Spike
W = Wave

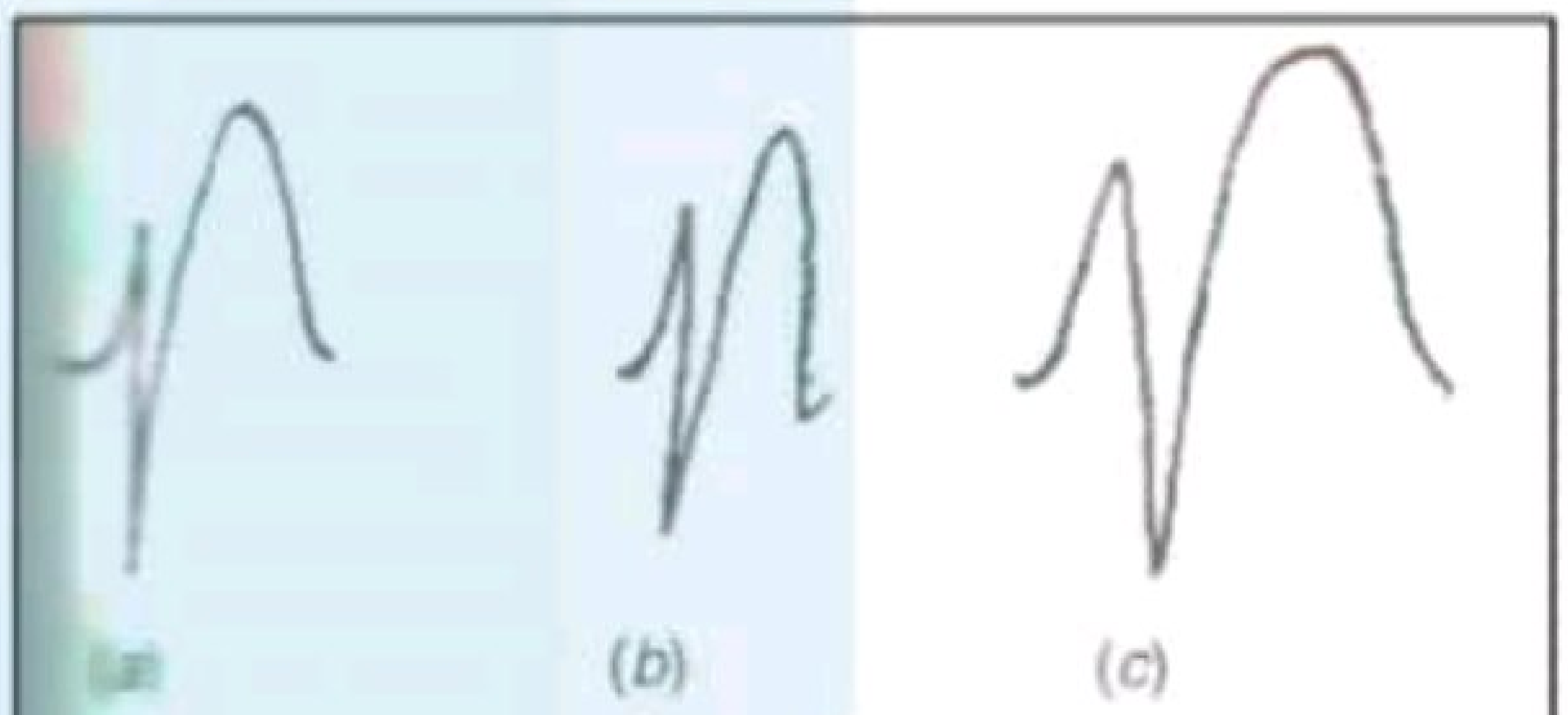
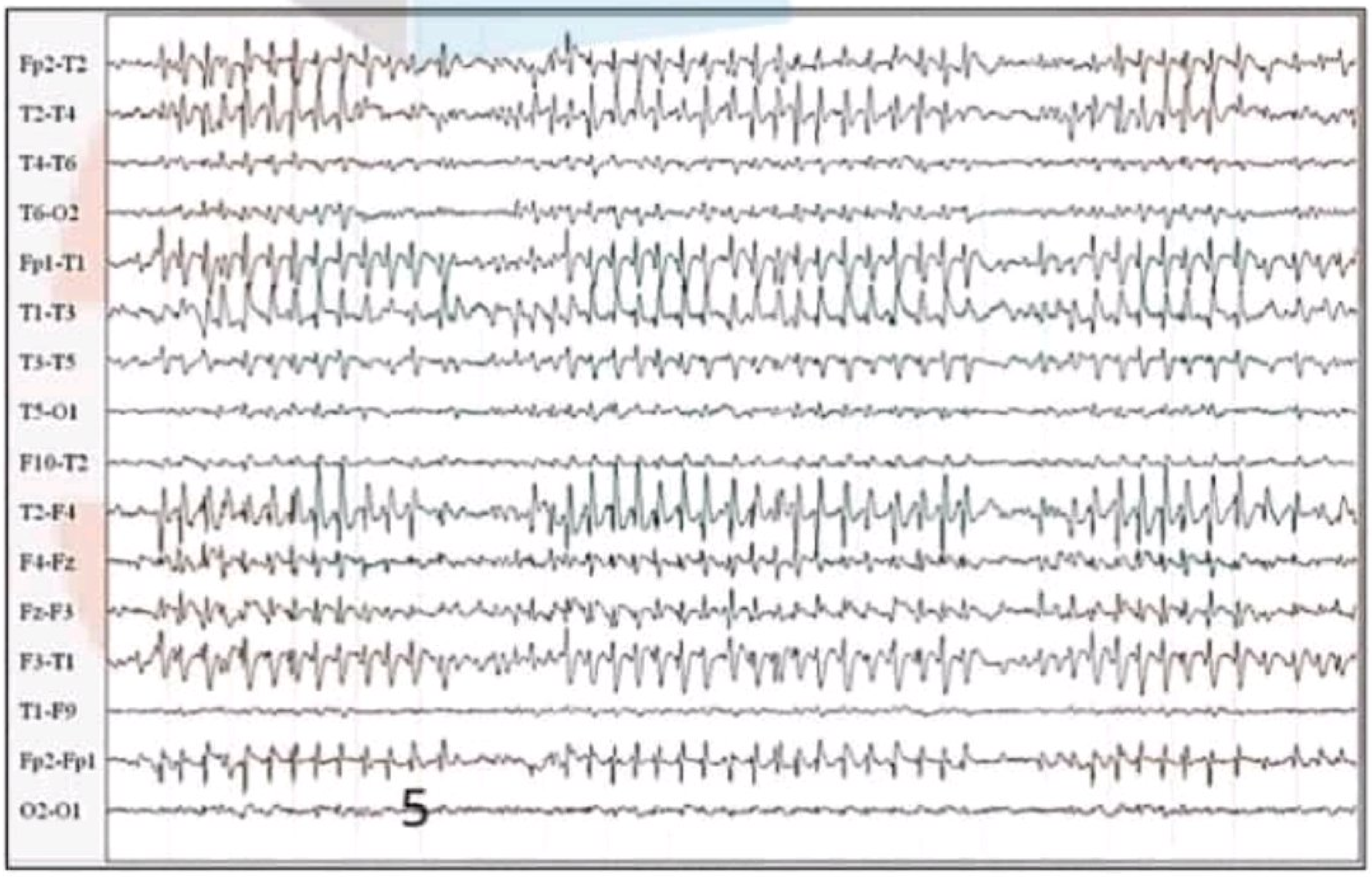


Fig. 5.7 *Schematic diagram of spike and slow wave complex (a) typical 3/sec, (b) fast (4–6/sec) and (c) slow (1–2.5/sec).*

Interpretation:

- 3 spike and waves in 1 second.
- Characteristic of **Absence Seizure.**


Fp2-T2
T2-T4
T4-T6
T6-O2
Fp1-T1
T1-T3
T3-T5
T5-O1
F10-T2
T2-F4
F4-Fz
Fz-F3
F3-T1
T1-F9
Fp2-Fp1
O2-O1

- **A seizure is said to be 'generalised' → when it's present in both hemisphere leads**
- **A seizure is said to be 'status' → when it is present for >5mins on EEG**

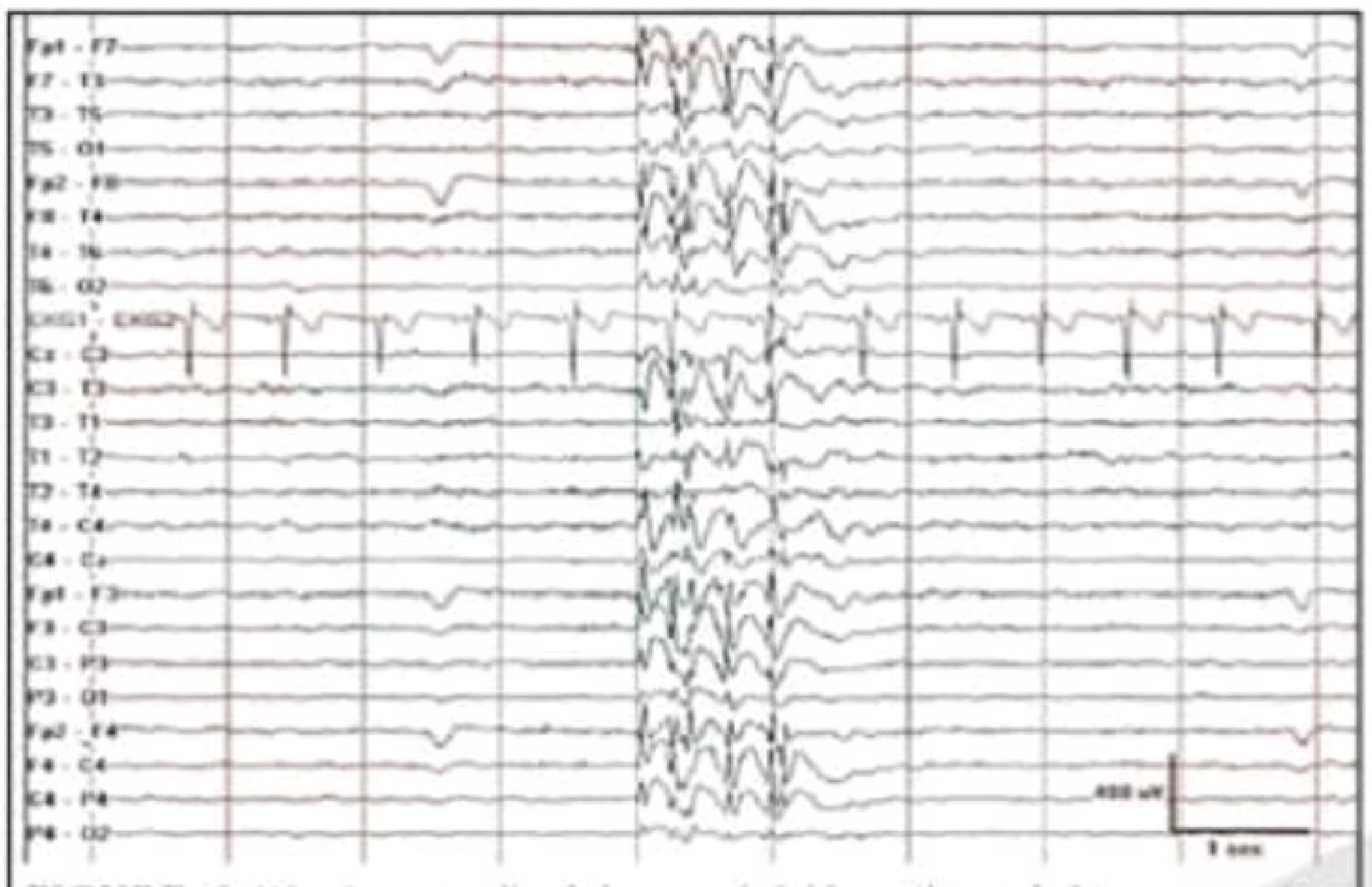


FIGURE 3.16. A generalized burst of 3-Hz spike-and-slow waves in a patient with IGE and absence seizures.

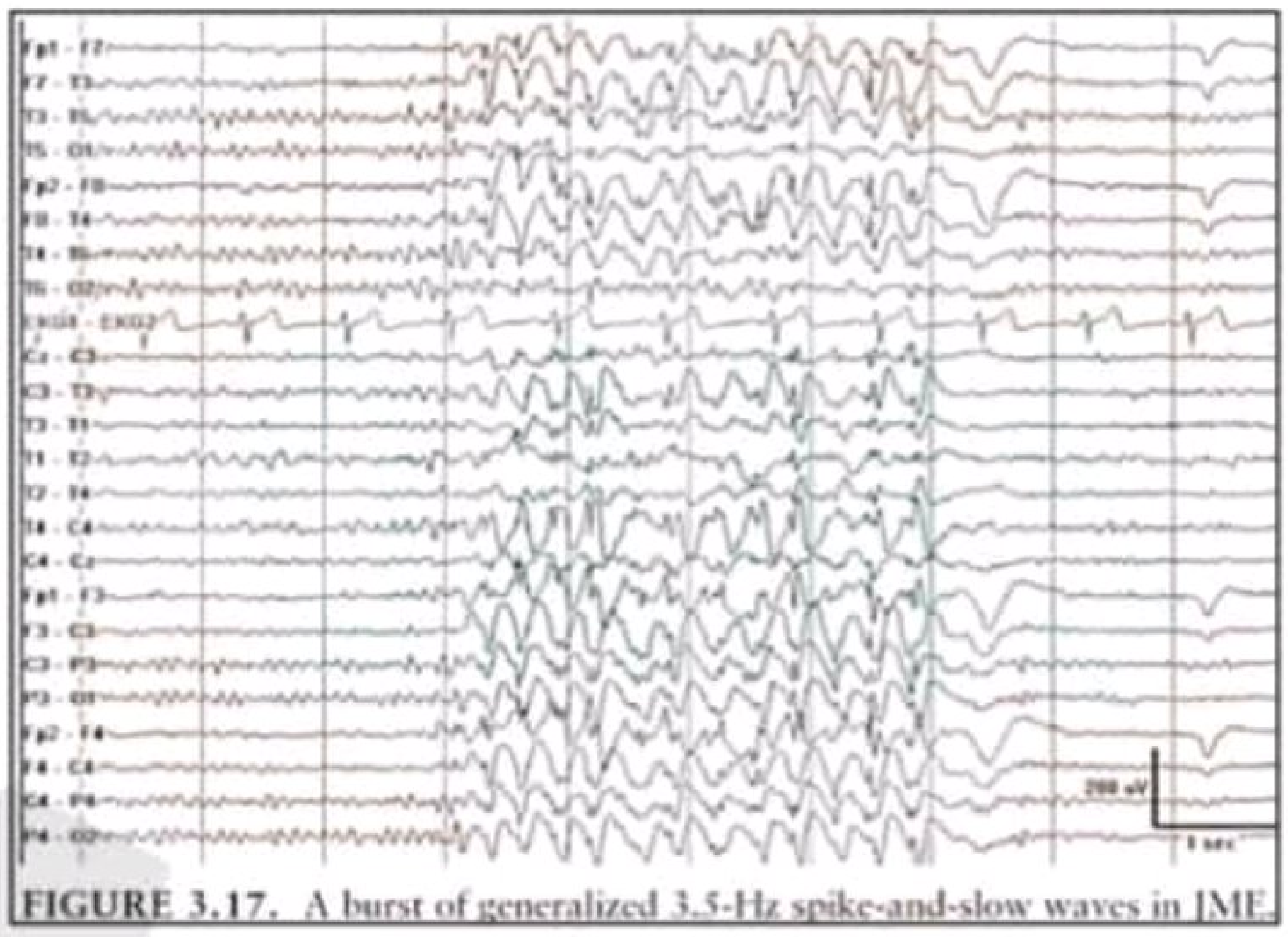


FIGURE 3.17. A burst of generalized 3.5-Hz spike-and-slow waves in JME.

- **Slow (<3Hz) Spike and Waves: LENNOX- GASTAUT Syndrome**
- **3/sec (3Hz) Spike and Waves: Absence seizure**
- **Fast (>3Hz) Spike and Waves: JME**

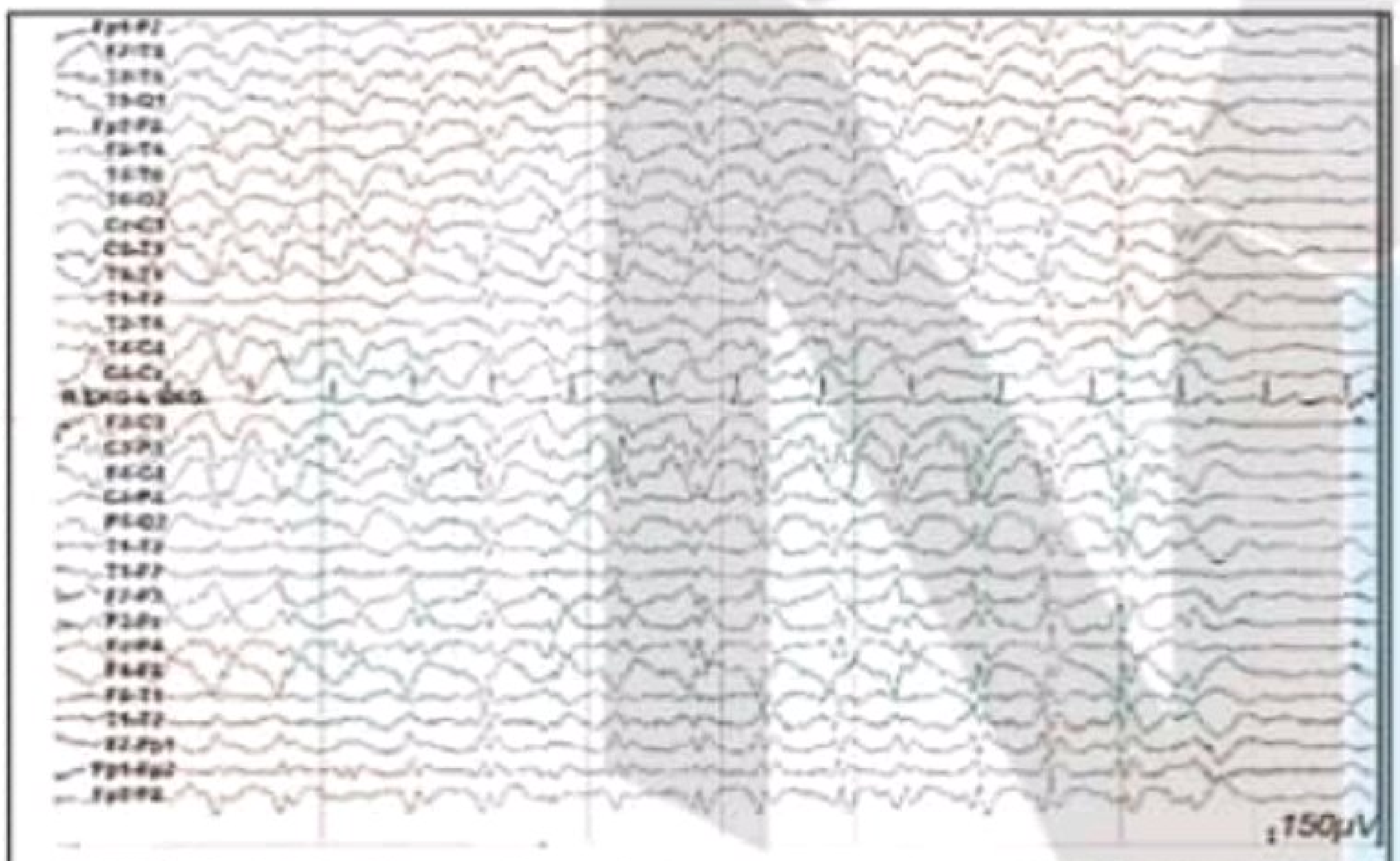


FIGURE 3.20. Slow-spike-and-wave in a patient with Lennox-Gastaut syndrome.

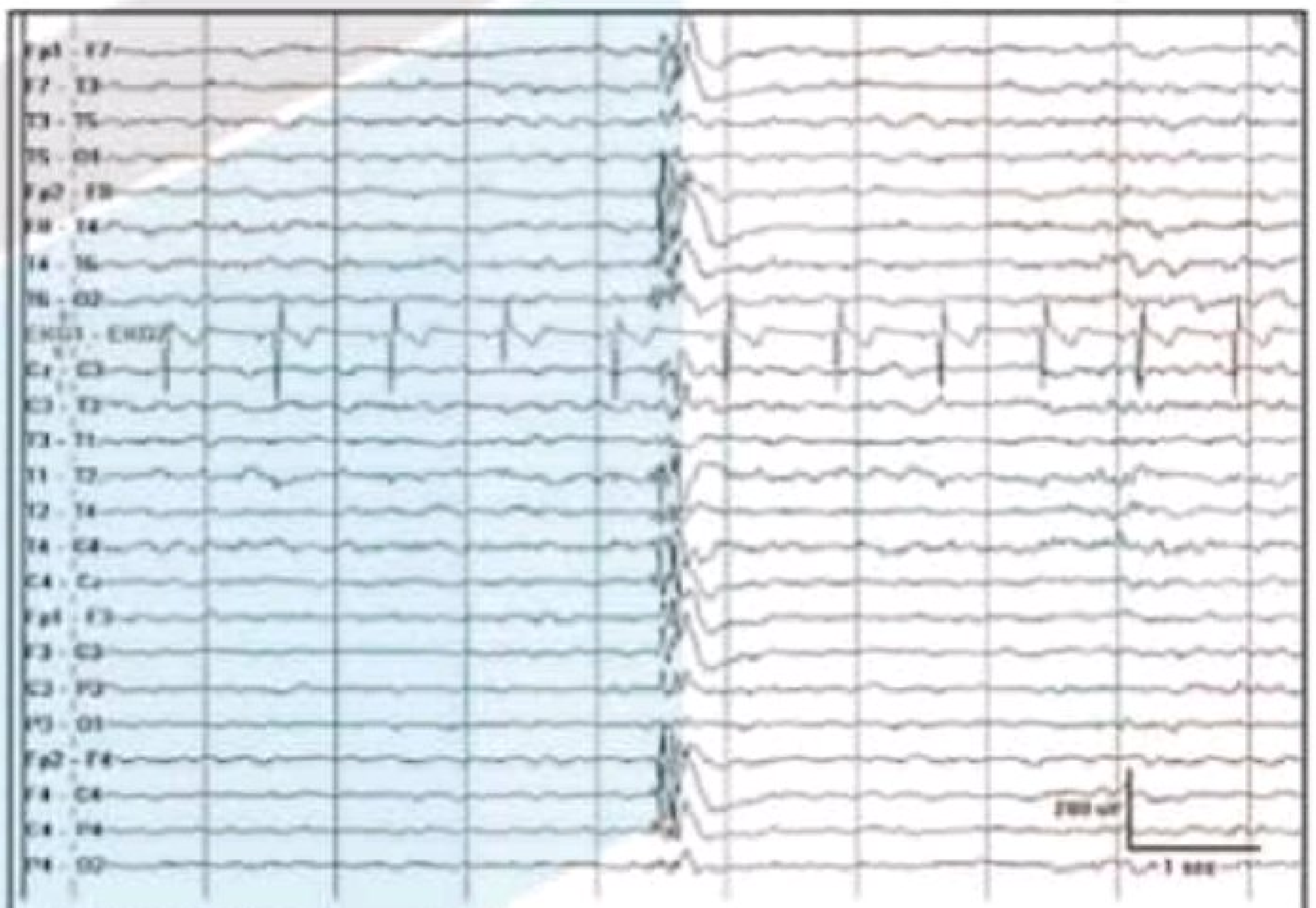
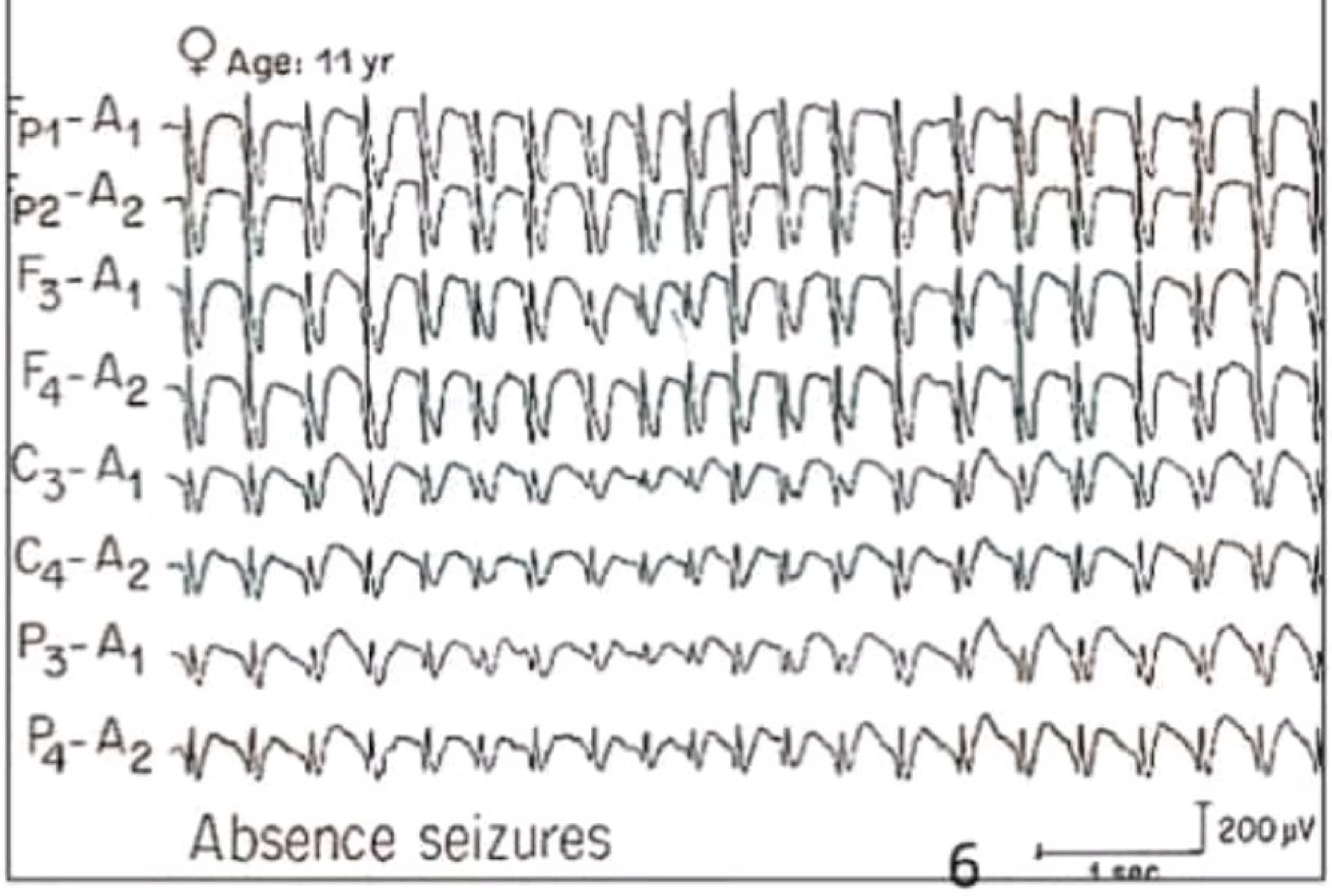


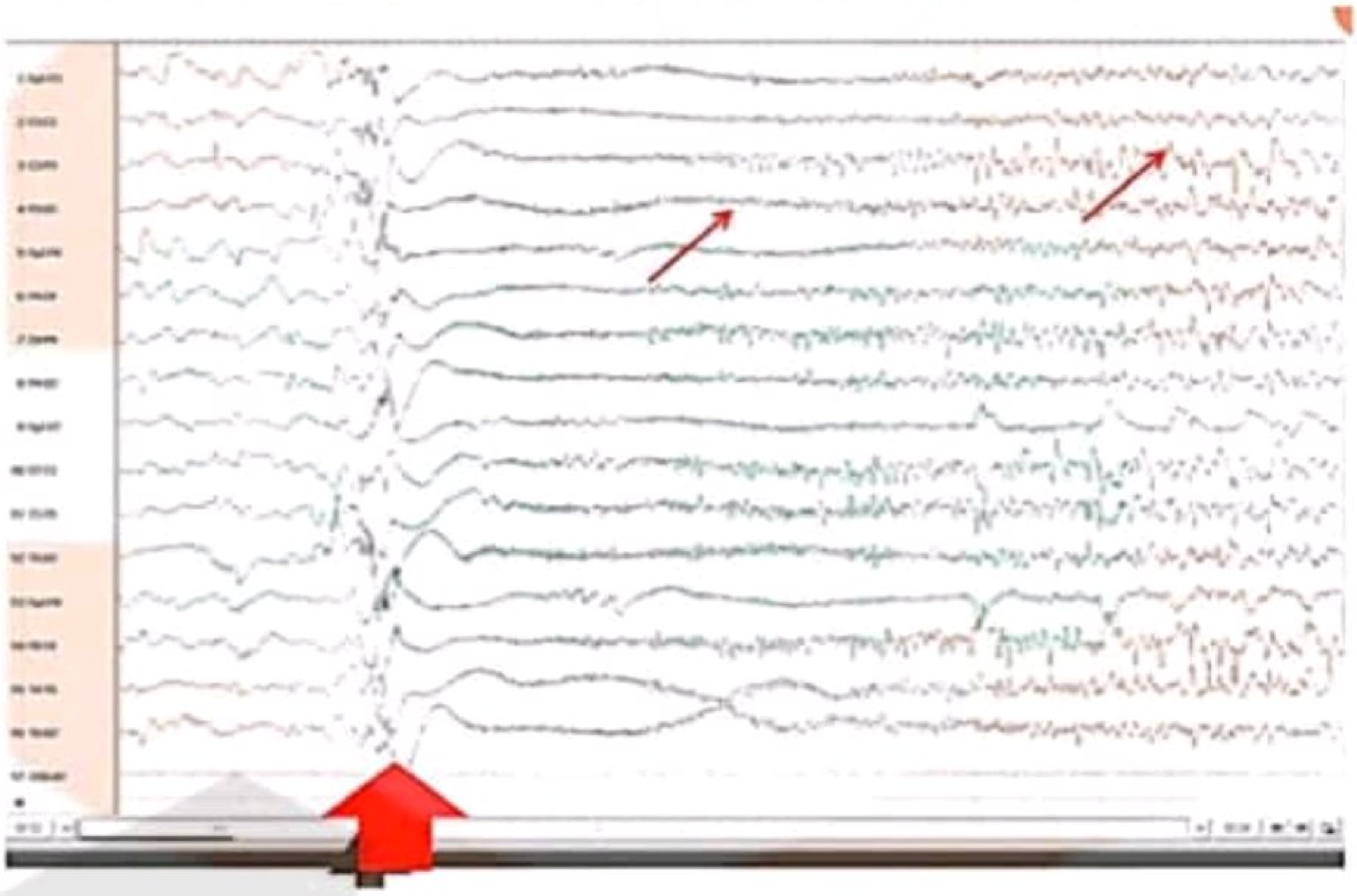
FIGURE 3.18. Generalized polyspike-and-slow wave in a patient with JME.

ABSENCE SEIZURE


♀ Age: 11 yr
Fp1-A1
Fp2-A2
F3-A1
F4-A2
C3-A1
C4-A2
P3-A1
P4-A2
Absence seizures
200 µV
1 sec

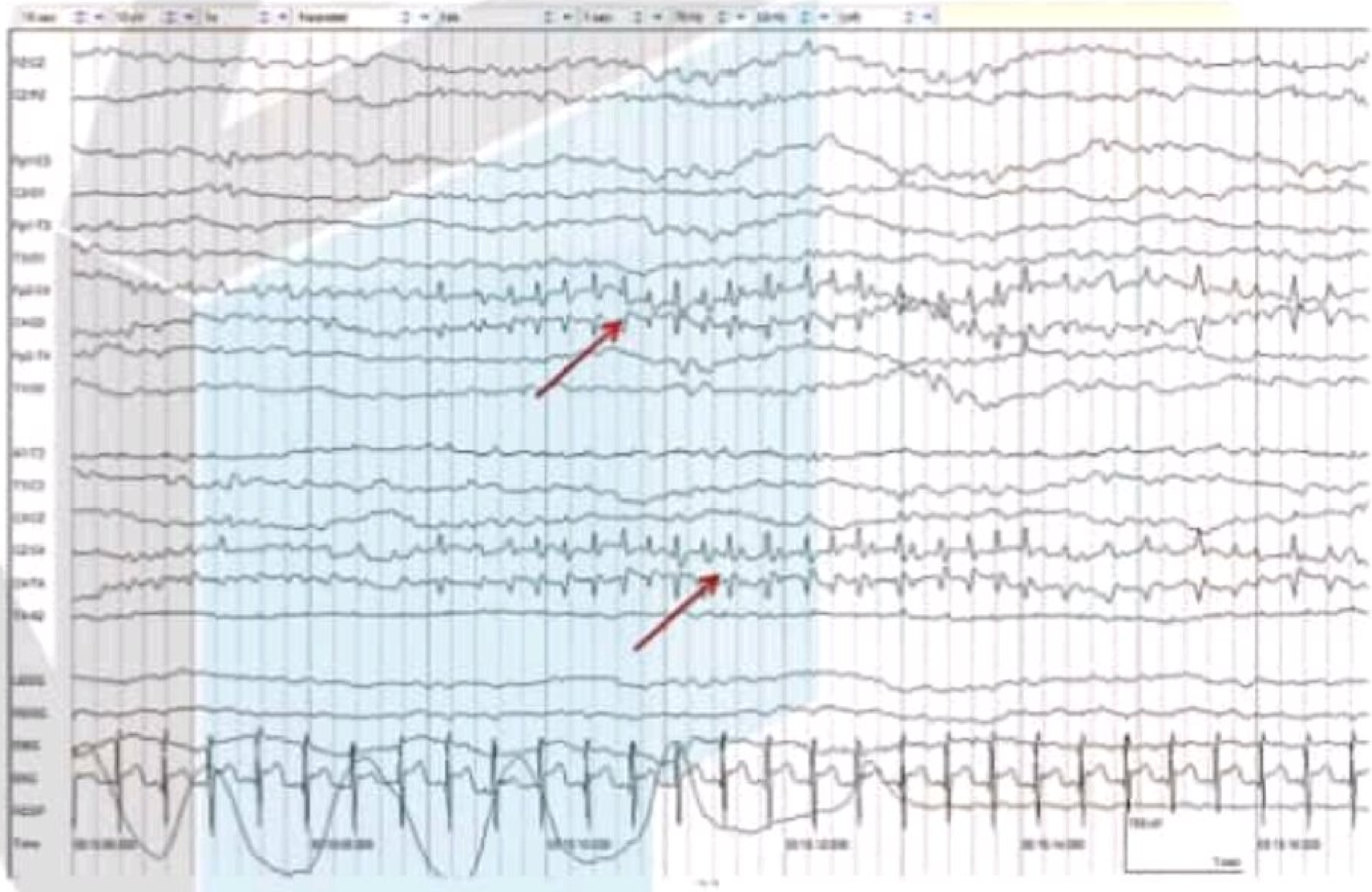
GENERALIZED TONIC CLONIC SEIZURE

- **Interpretation- GTCS**
  - Epileptogenic seizure activity followed by slowing of the waveforms



PARTIAL SEIZURE

- **Interpretation- Partial Seizure**
  - Epileptogenic seizure activity is present in right sided leads but absent in left sided leads.



CONCEPT OF FORCED NORMALIZATION

- A group of patients with poorly controlled epilepsy who had psychotic episodes associated with remission of their seizure and disappearance of epileptiform activity on their EEGs. This concept is called as **FORCED NORMALIZATION**
- Therefore, the anti-epileptic drug having better seizure control will have more behavioural abnormality. (Same concept in ECT- Give Seizure to control psychosis)

Forced Normalization
- A Putative Model

- "Forced Normalization is the phenomenon characterised by the fact that, with the occurrence of the psychotic states, the EEG becomes more normal or entirely normal as compared with previous and subsequent EEG findings"
- Put more crudely, "there would seem to be epileptics who must have a pathological EEG in order to be mentally sane"

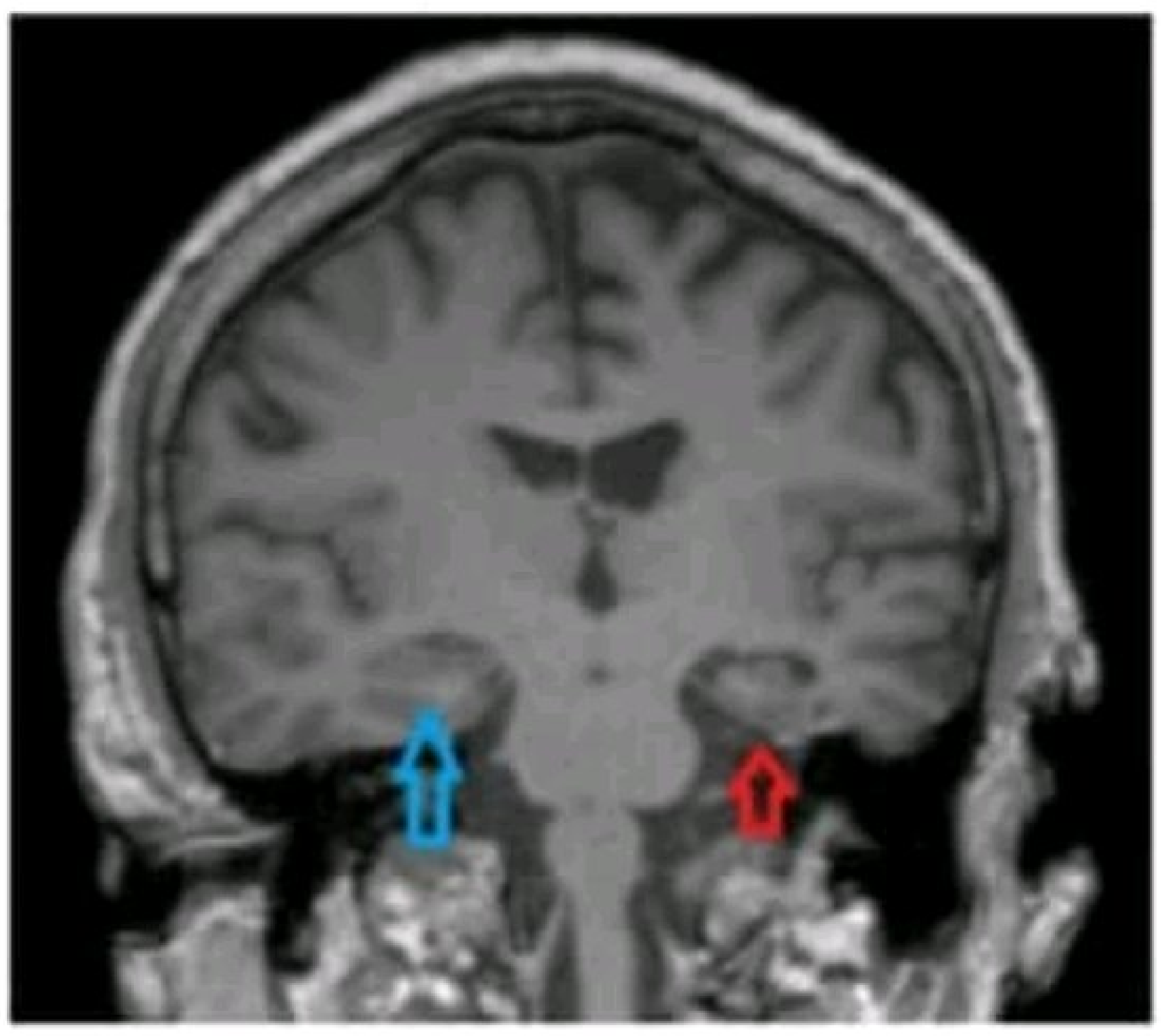
- **Seizure is a hypo-dopaminergic state (↑sed Prolactin) whereas Psychosis is a HYPERdopaminergic state.**
- The appearance of psychosis may coincide with cessation of seizure **(alternative psychosis)** and the loss of paroxysmal abnormalities on EEG (Forced Normalization)

RADIOLOGY

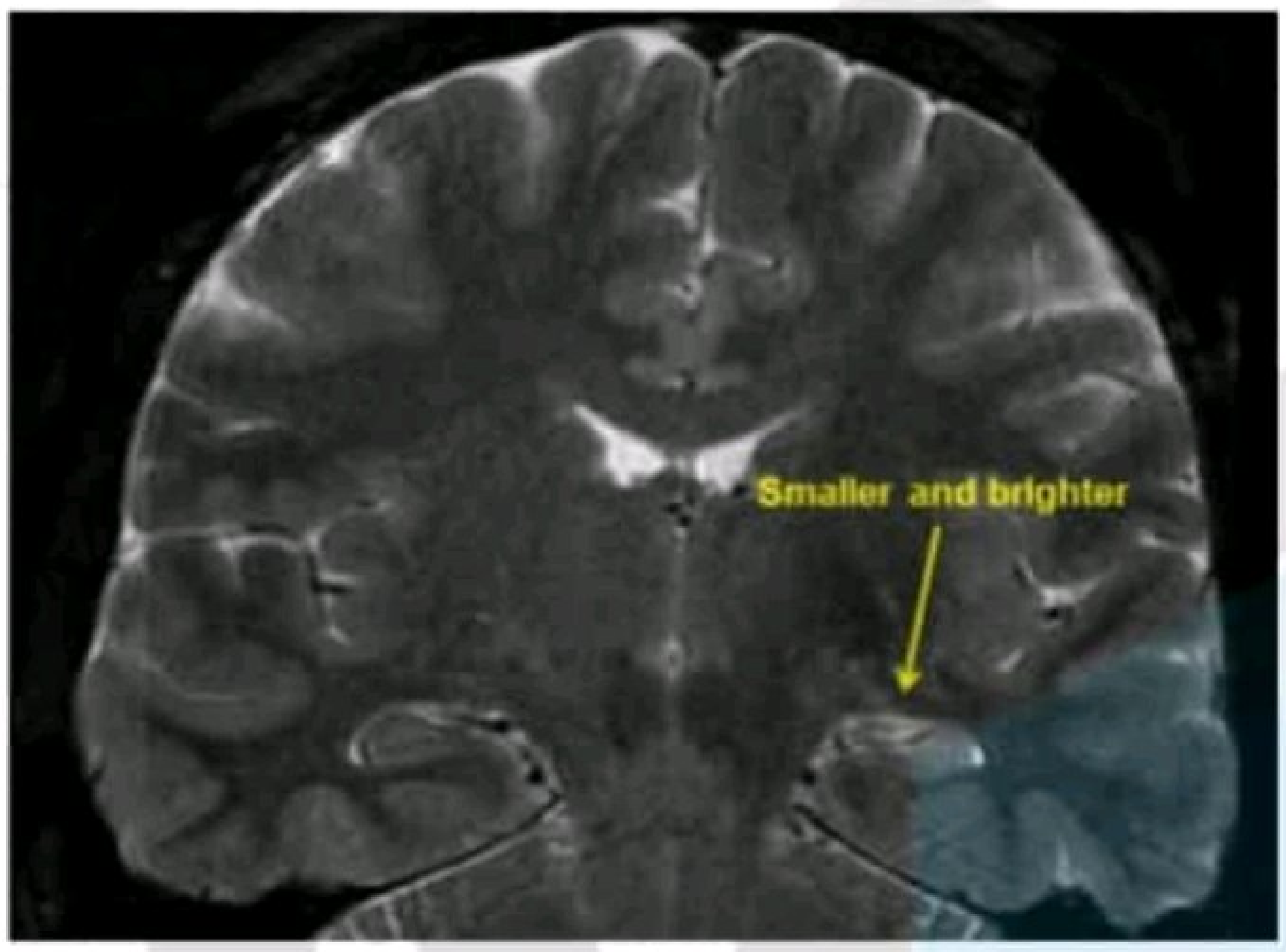
MRI- Oblique Coronal Section done in

COMPLEX PARTIAL SEIZURE

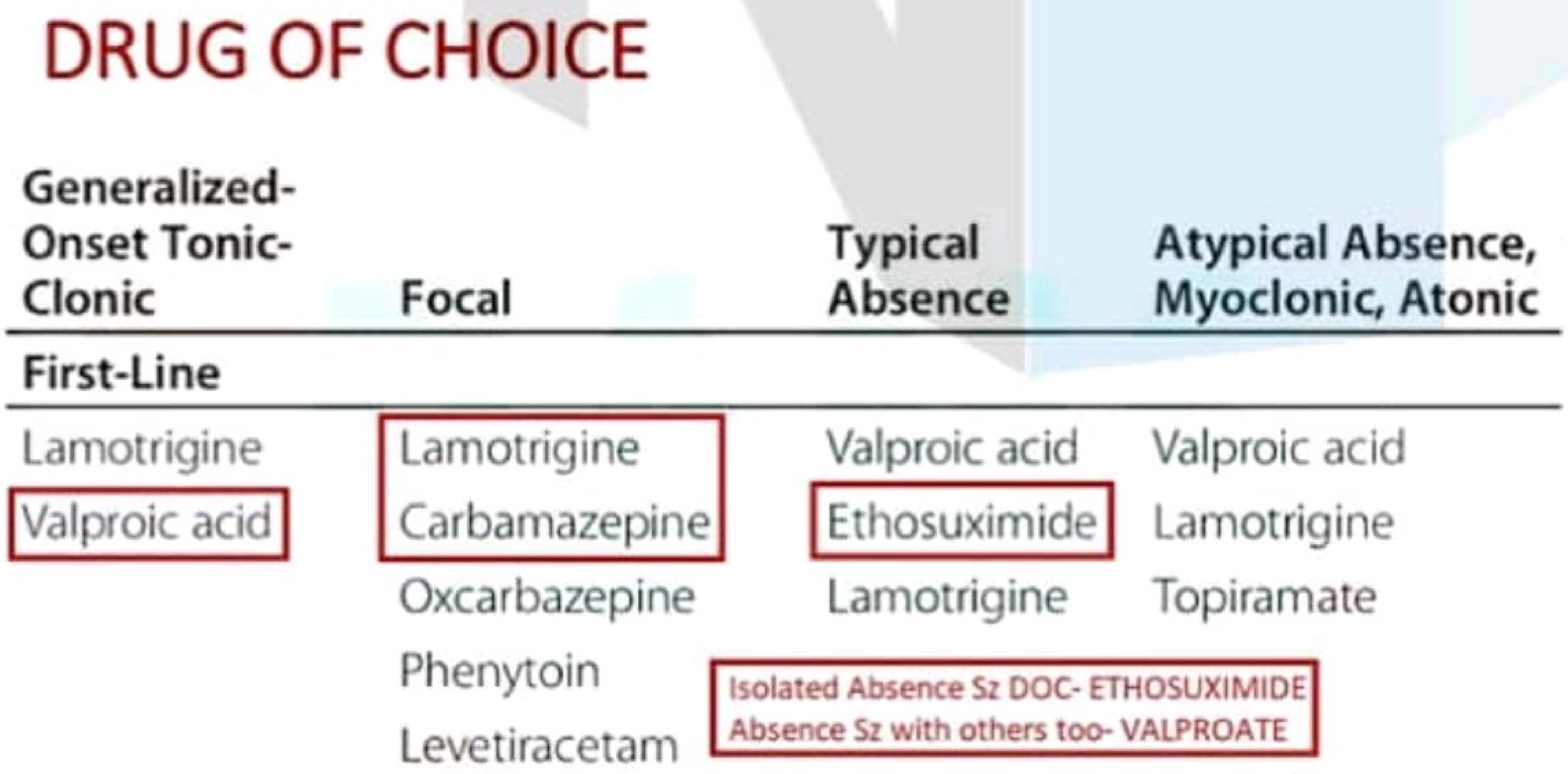
Findings: **Mesial temporal sclerosis.** RED arrow is the pathological side showing widening of the inferior horn of lateral ventricle due to atrophy of the hippocampus.



Abnormal Hippocampus appearing smaller and brighter.



PHARMACOLOGY: ANTI-EPILEPTIC DRUGS



DRUG OF CHOICE

Generalized-Onset Tonic-Clonic	Focal	Typical Absence	Atypical Absence, Myoclonic, Atonic
First-Line			
Lamotrigine Valproic acid	Lamotrigine Carbamazepine Oxcarbazepine Phenytoin Levetiracetam	Valproic acid Ethosuximide Lamotrigine	Valproic acid Lamotrigine Topiramate

Isolated Absence Sz DOC- ETHOSUXIMIDE
Absence Sz with others too- VALPROATE

PREGNANCY	CONTINUE OLD DRUG NEW DRUG (SAFETY): OXCARBAZEPINE > LEVETIRACETAM > LAMOTRIGINE
FEBRILE SEIZURES	DIAZEPAM (RECTAL, IV, INTRANASAL) MIDAZOLAM (INTRANASAL)
INFANTILE SPASM	ACTH +/- CORTICOSTEROIDS
INFANTILE SPASM + TUBEROUS SCLEROSIS	VIGABATRIN **(S/E: BILATERAL VISUAL FIELD CONTRACTION)**
LENNOX GESTAUT SYNDROME	VALPROATE (DOC) NEW DRUGS: RUFINAMIDE, FELBAMATE
DRAVETS SYNDROME	VALPROATE (DOC) NEW DRUG: STIRIPENTOL
STATUS EPILEPTICUS	LORAZEPAM (OR OTHER BENZODIAZEPINES)

Continue the old drug (even if teratogenic). Otherwise it can cause Rebound Sz → Status

Orphan drugs:

RUFINAMIDE
FELBAMATE
STIRIPENTOL

CLASSIFICATION OF ANTIEPILEPTICS

BLOCK USE DEPENDANT VOLTAGE GATED Na^+ CHANNELS	**PHENYTOIN. CARBAMAZEPINE. VALPROATE. RUFINAMIDE**	**TOPIRAMATE LAMOTRIGINE LACOSAMIDE, ZONISAMIDE, .**
BLOCK "T" TYPE OF CALCIUM CHANNELS	**VALPROATE ETHOSUXIMIDE LAMOTRIGINE ZONISAMIDE CLONAZEPAM**	
GABA AGONIST	**BARBITURATES, BENZODIAZEPINE**	
GABA TRANSAMINASE INHIBITOR	**VIGABATRIN, VALPROATE**	
GABA TRANSPORTER INHIBITOR	**TIAGABINE**	
NMDA BLOCKER	**FELBAMATE**	
AMPA BLOCKER	**PERAMPANEL, TELAMPANEL**	

SIDE EFFECTS

1. PHENYTOIN

HIRSUTISM, HYPERPLASIA OF GUMS OSTEOMALACIA
TERATOGENIC: CLEFT LIP/PALATE

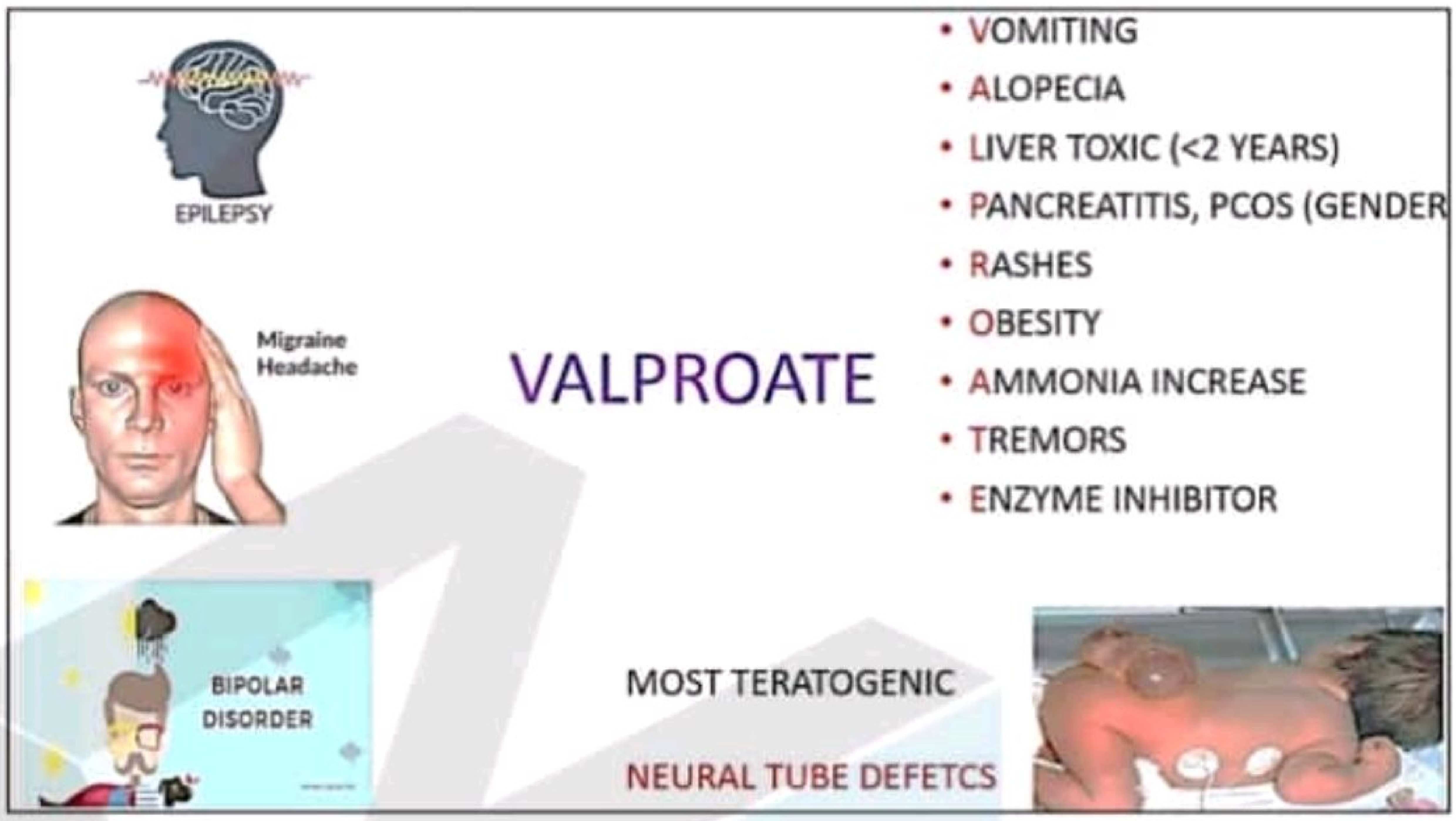
MEGALOBLASTIC ANEMIA
ARRHYTHMIA
LYMPHADENOPATHY
INHIBIT INSULIN RELEASE
K VITAMIN DEFICIENCY
ATAXIA, DIPLOPIA, NYSTAGMUS

2. CARBAMAZEPINE

STEVEN JHONSON/RASH
HEPATOTOXIC
APLASTIC ANEMIA
DIPLOPIA, ATAXIA
EOSINOPHILIA
SIADH

3. Uses of Valproate:

- **Epilepsy**
- **Migraine**
- **Bipolar d/o**


EPILEPSY
Migraine Headache
BIPOLAR DISORDER

VALPROATE

- VOMITING
- ALOPECIA
- LIVER TOXIC (<2 YEARS)
- PANCREATITIS, PCOS (GENDER
- RASHES
- OBESITY
- AMMONIA INCREASE
- TREMORS
- ENZYME INHIBITOR

MOST TERATOGENIC

NEURAL TUBE DEFETCS

4. TOPIRAMATE, ZONISAMIDE

S/E: 1) Weight loss (Used as an Anti-Obesity drug)

2) Kidney Stones

3) Angle Closure Glaucoma

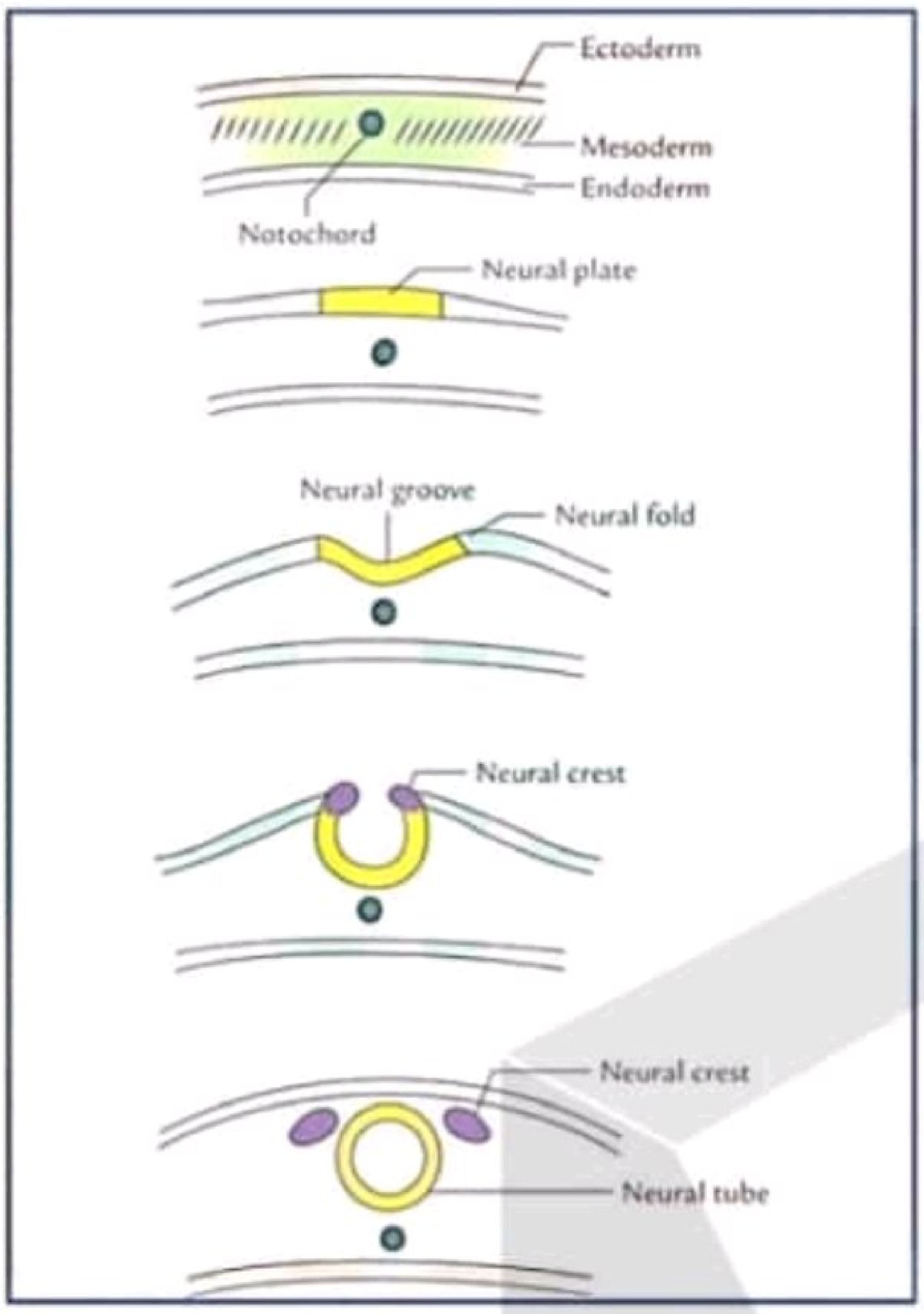
5. LEVETIRACETAM, BRIVARACETAM

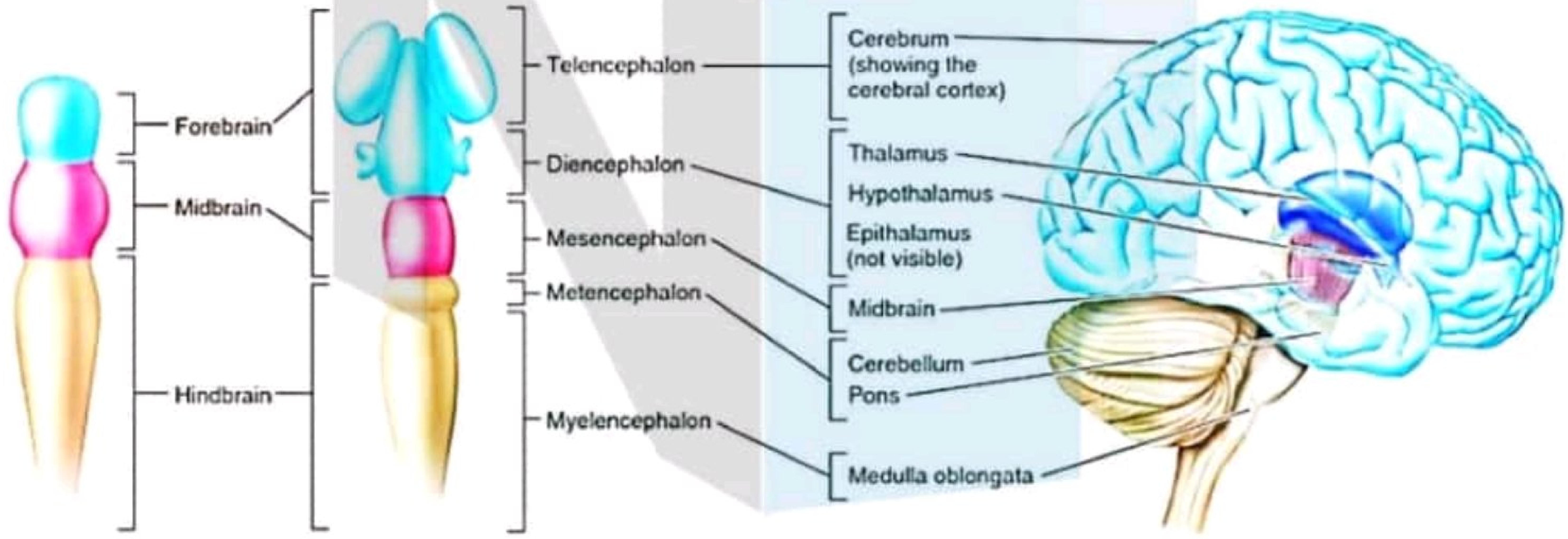
SV2A Inhibitor, Nootrophic (Increased memory) and Antioxidant

6. VIGABATRIN

S/E- Bilateral Visual Field defects

NEUROANATOMY

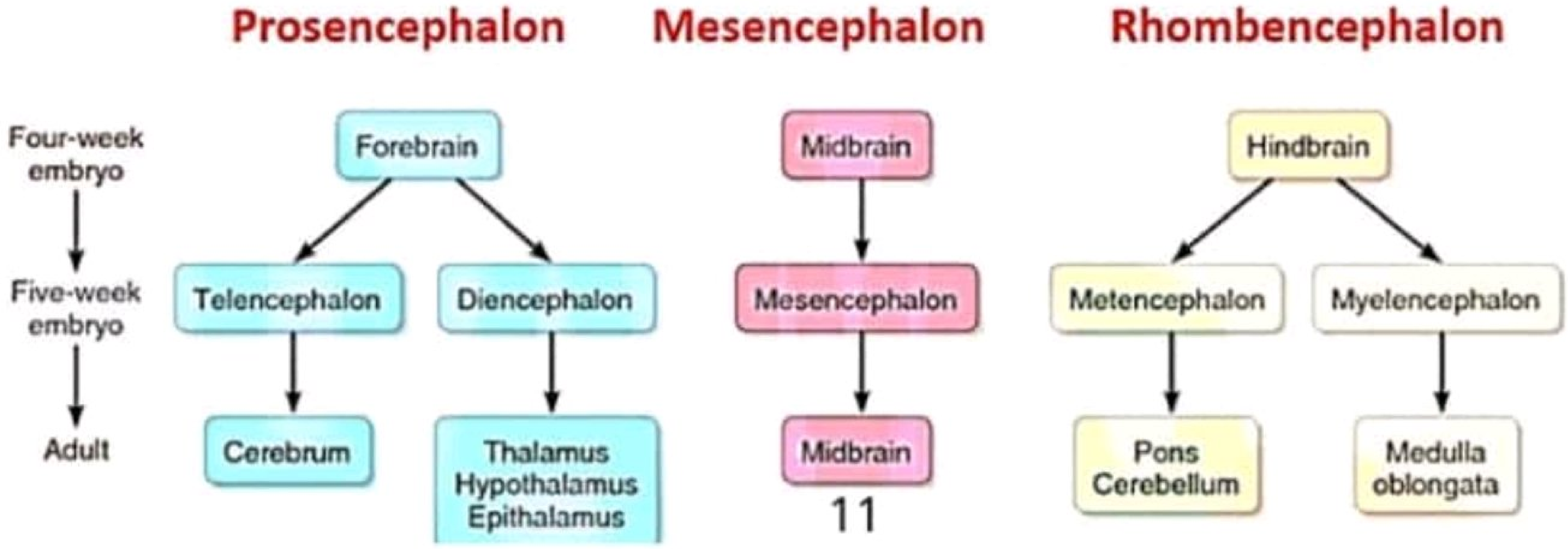

Ectoderm
Mesoderm
Endoderm
Notochord
Neural plate
Neural groove
Neural fold
Neural crest
Neural crest
Neural tube


Forebrain
Midbrain
Hindbrain
Telencephalon
Diencephalon
Mesencephalon
Metencephalon
Myelencephalon
Cerebrum (showing the cerebral cortex)
Thalamus
Hypothalamus
Epithalamus (not visible)
Midbrain
Cerebellum
Pons
Medulla oblongata

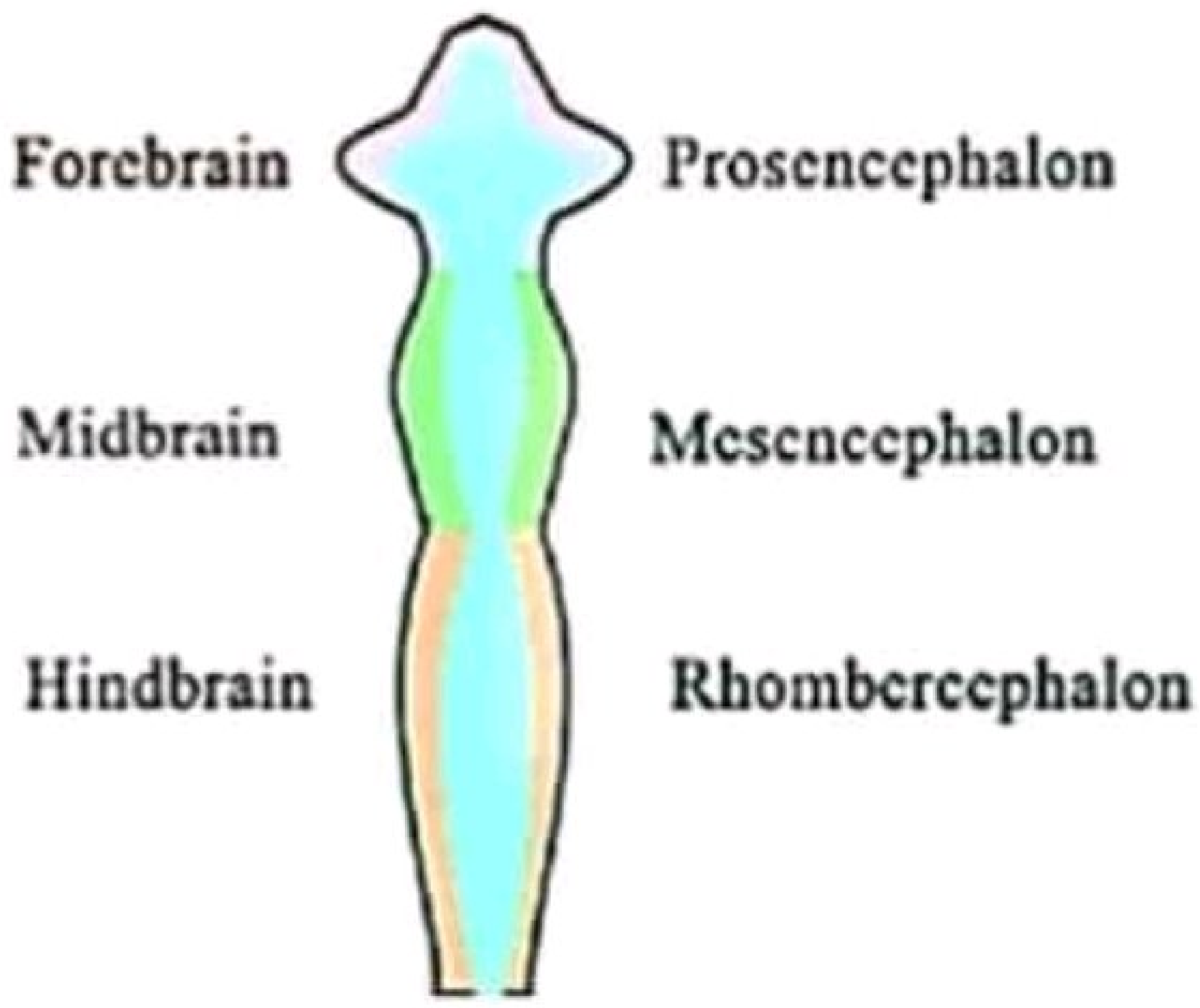
(a) Embryo brain (four weeks)

(b) Embryo brain (five weeks)

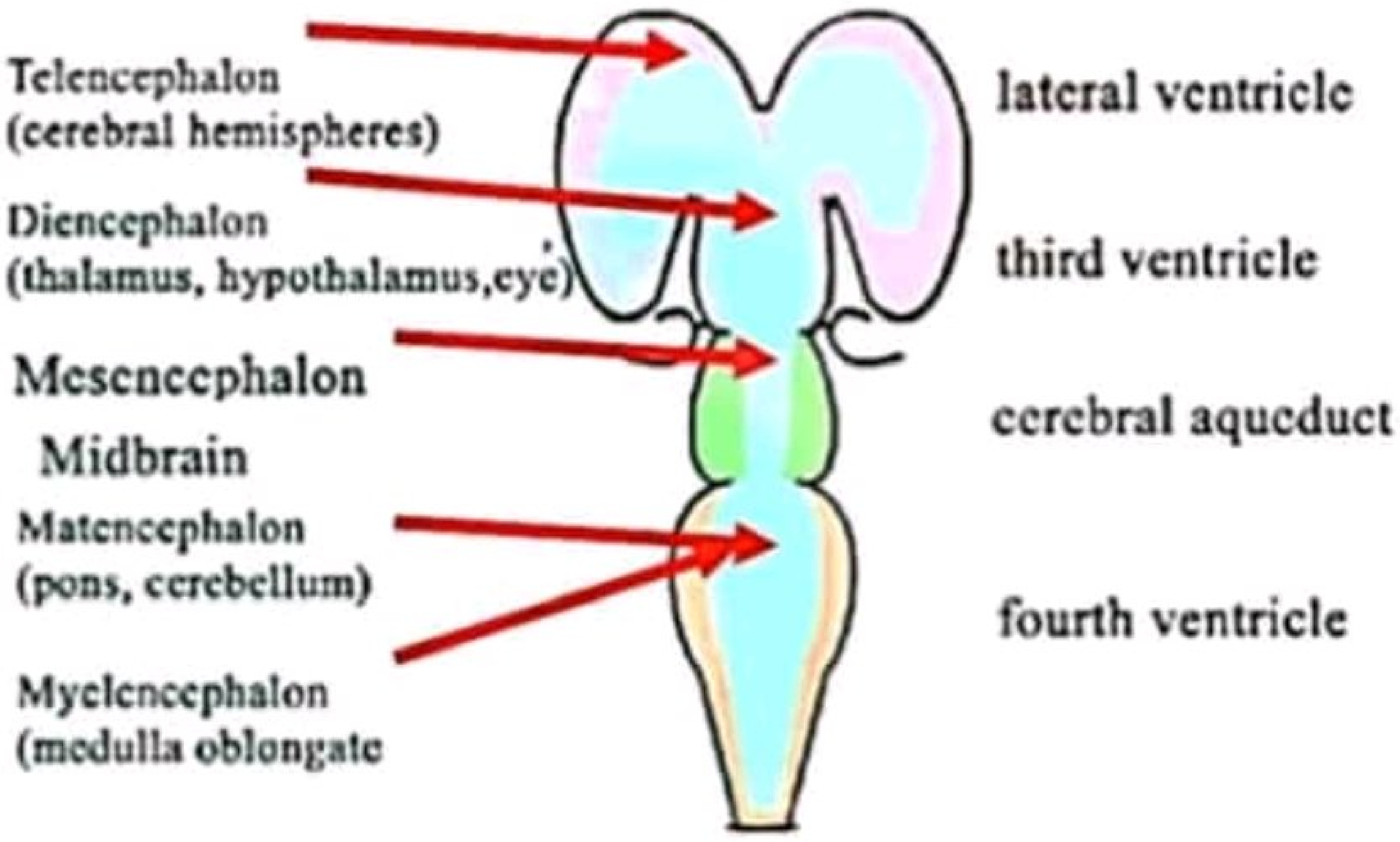
(c) Adult brain

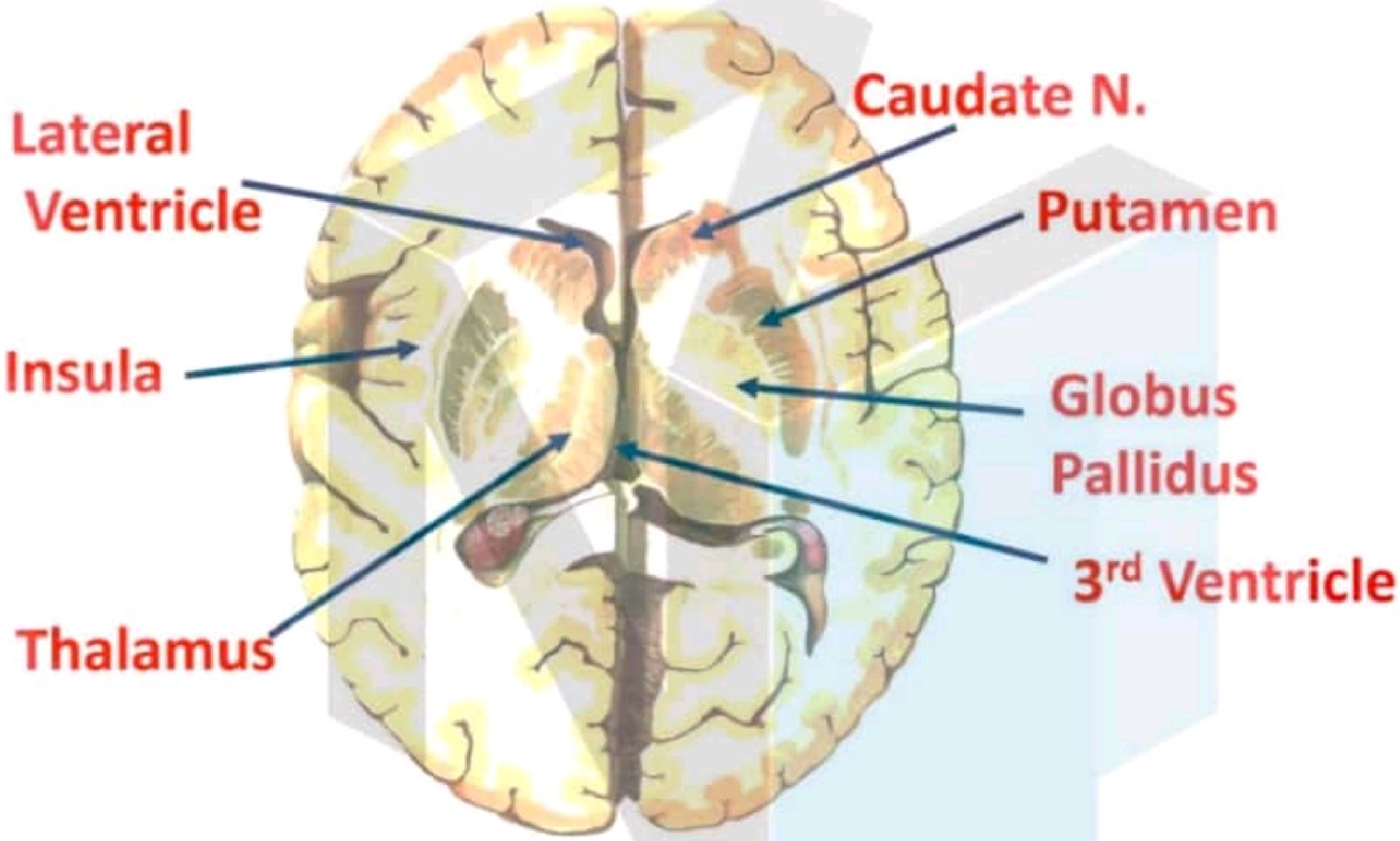

Prosencephalon
Mesencephalon
Rhombencephalon
Four-week embryo
Five-week embryo
Adult
Forebrain
Telencephalon
Diencephalon
Cerebrum
Thalamus
Hypothalamus
Epithalamus
Midbrain
Mesencephalon
Midbrain
Hindbrain
Metencephalon
Myelencephalon
Pons
Cerebellum
Medulla oblongata

1st stage -3 vesicles


Forebrain
Prosencephalon
Midbrain
Mesencephalon
Hindbrain
Rhomberecephalon

2nd stage -5 vesicles


Telencephalon
(cerebral hemispheres)
Diencephalon
(thalamus, hypothalamus,eye)
Mesencephalon
Midbrain
Matencephalon
(pons, cerebellum)
Myelencephalon
(medulla oblongate
lateral ventricle
third ventricle
cerebral aqueduct
fourth ventricle


Lateral Ventricle
Caudate N.
Putamen
Insula
Globus Pallidus
3rd Ventricle
Thalamus

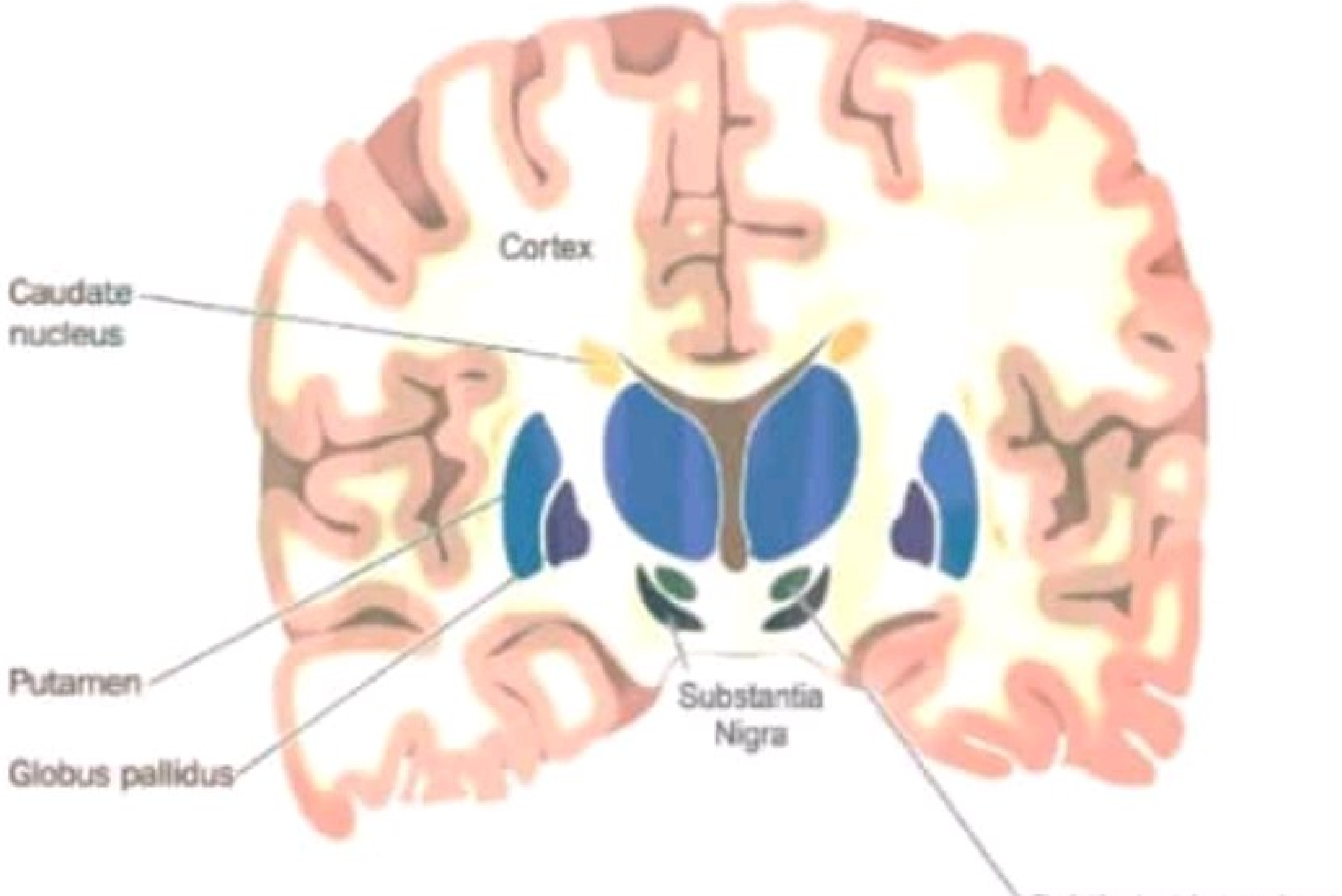
CORPUS STRIATUM

= Caudate Nucleus + Putamen+ Lentiform Nucleus

STRIATUM

= Caudate Nucleus + Putamen

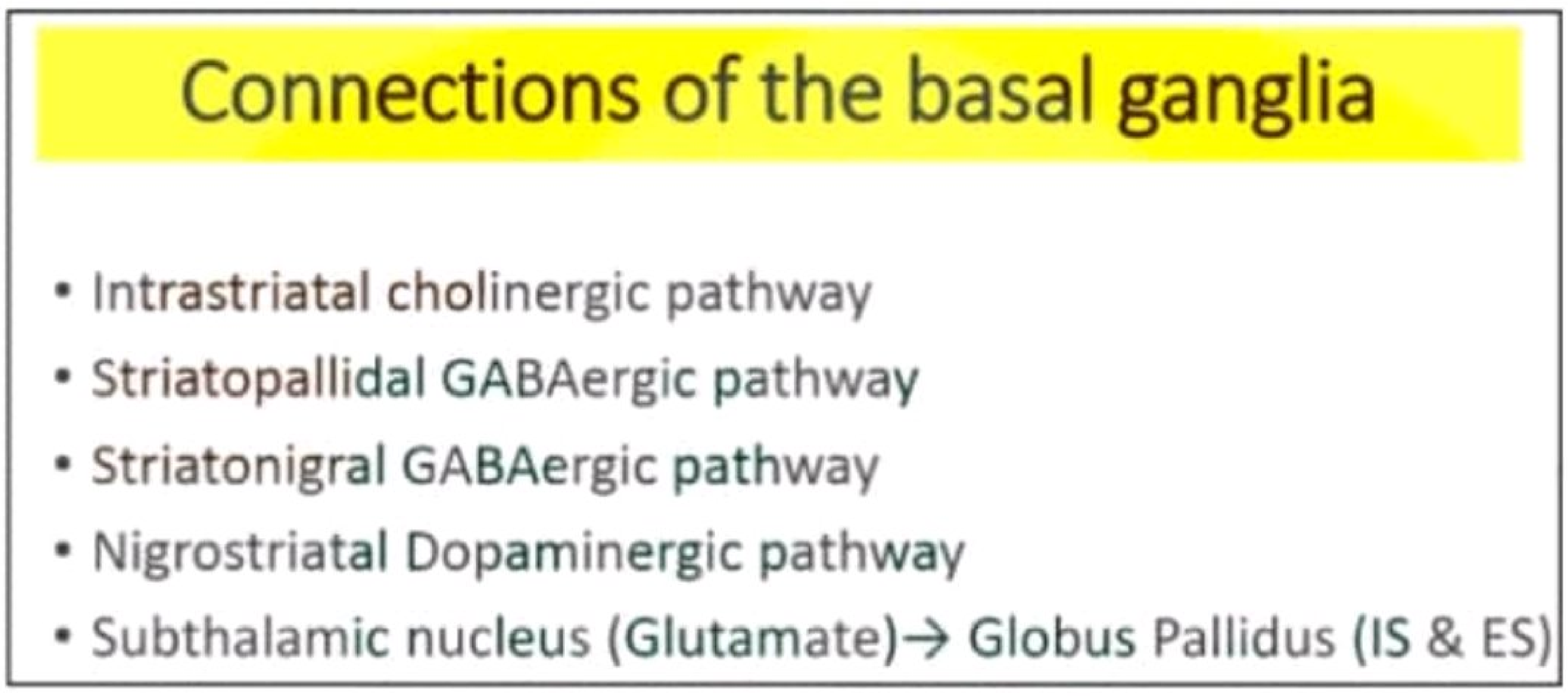
Parts of basal ganglia and neurotransmitters secreted by them


Cortex
Caudate nucleus
Putamen
Globus pallidus
Substantia Nigra
Subthalamic nucleus

Glutamate is the only excitatory Neurotransmitter secreted by Basal Ganglia which is secreated by Subthalamus

STRIATE secretes:

- GABA 95%
- ACh 5%
- Somatostatin

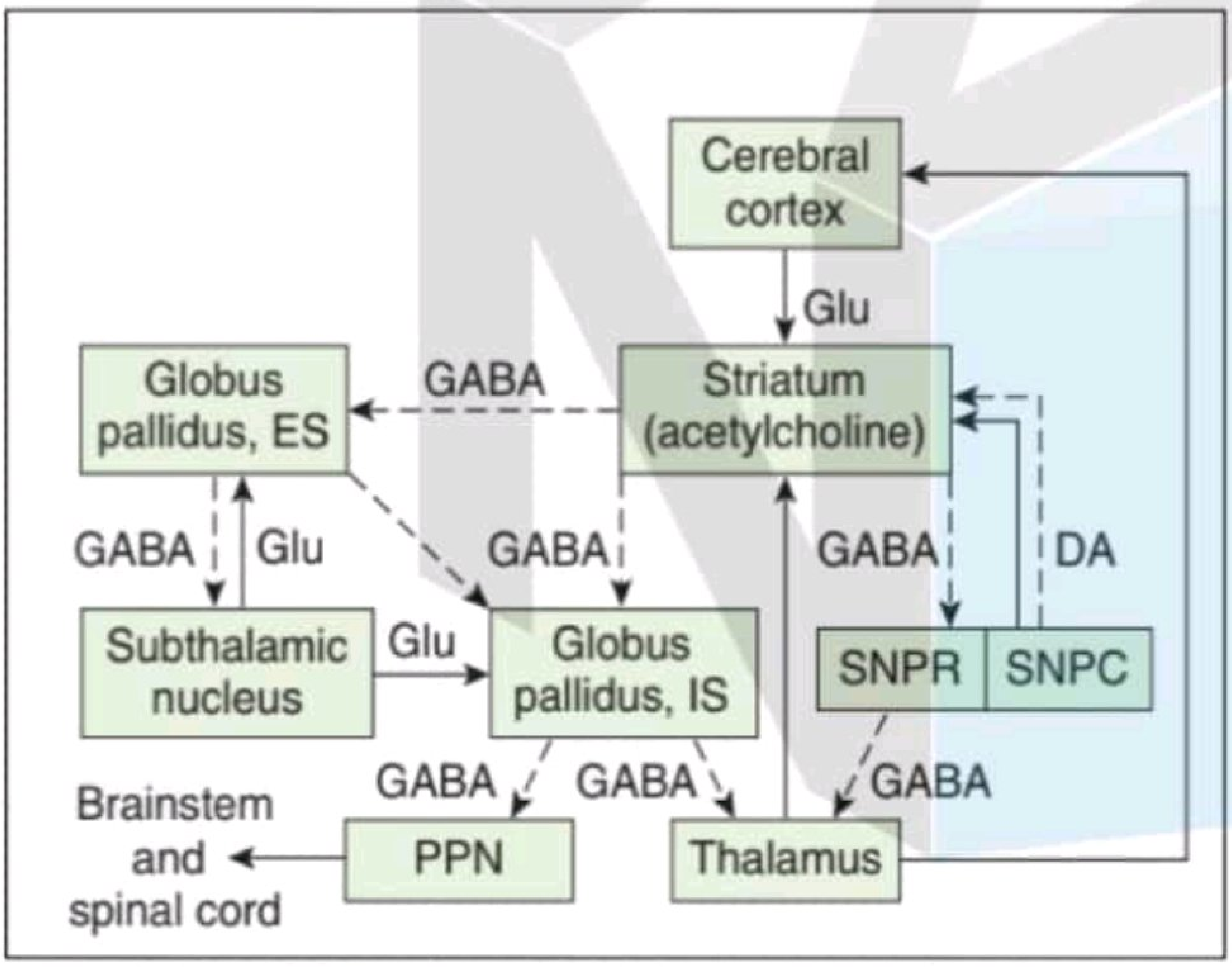


Connections of the basal ganglia

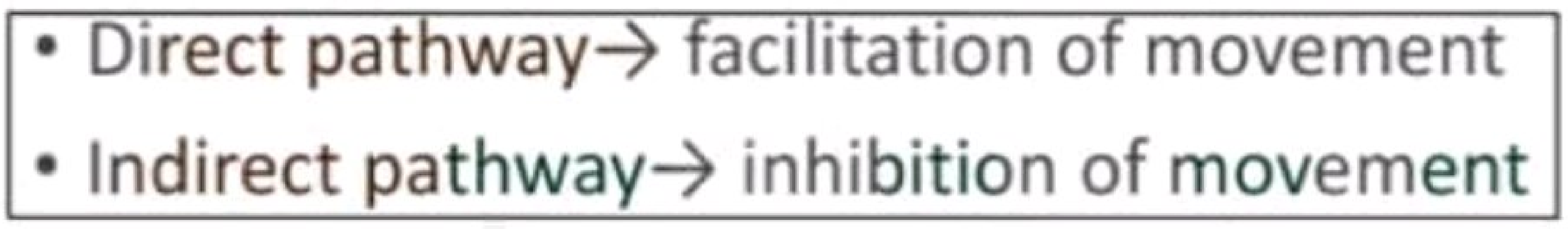
- Intrastriatal cholinergic pathway
- Striatopallidal GABAergic pathway
- Striatonigral GABAergic pathway
- Nigrostriatal Dopaminergic pathway
- Subthalamic nucleus (Glutamate)→ Globus Pallidus (IS & ES)

- GLOBUS PALLIDUS (Both Internal & External segment): GABA
- Substantia Nigra Pars reticulata: GABA
- Substantia Nigra Pars compacta: Dopamine

Q- Dopaminergic Receptors (D1 & D2) are present over STRIATUM


Cerebral cortex
Glu
Globus pallidus, ES
GABA
Striatum (acetylcholine)
GABA
Glu
GABA
GABA
DA
Subthalamic nucleus
Glu
Globus pallidus, IS
SNPR
SNPC
GABA
GABA
GABA
Brainstem and spinal cord
PPN
Thalamus

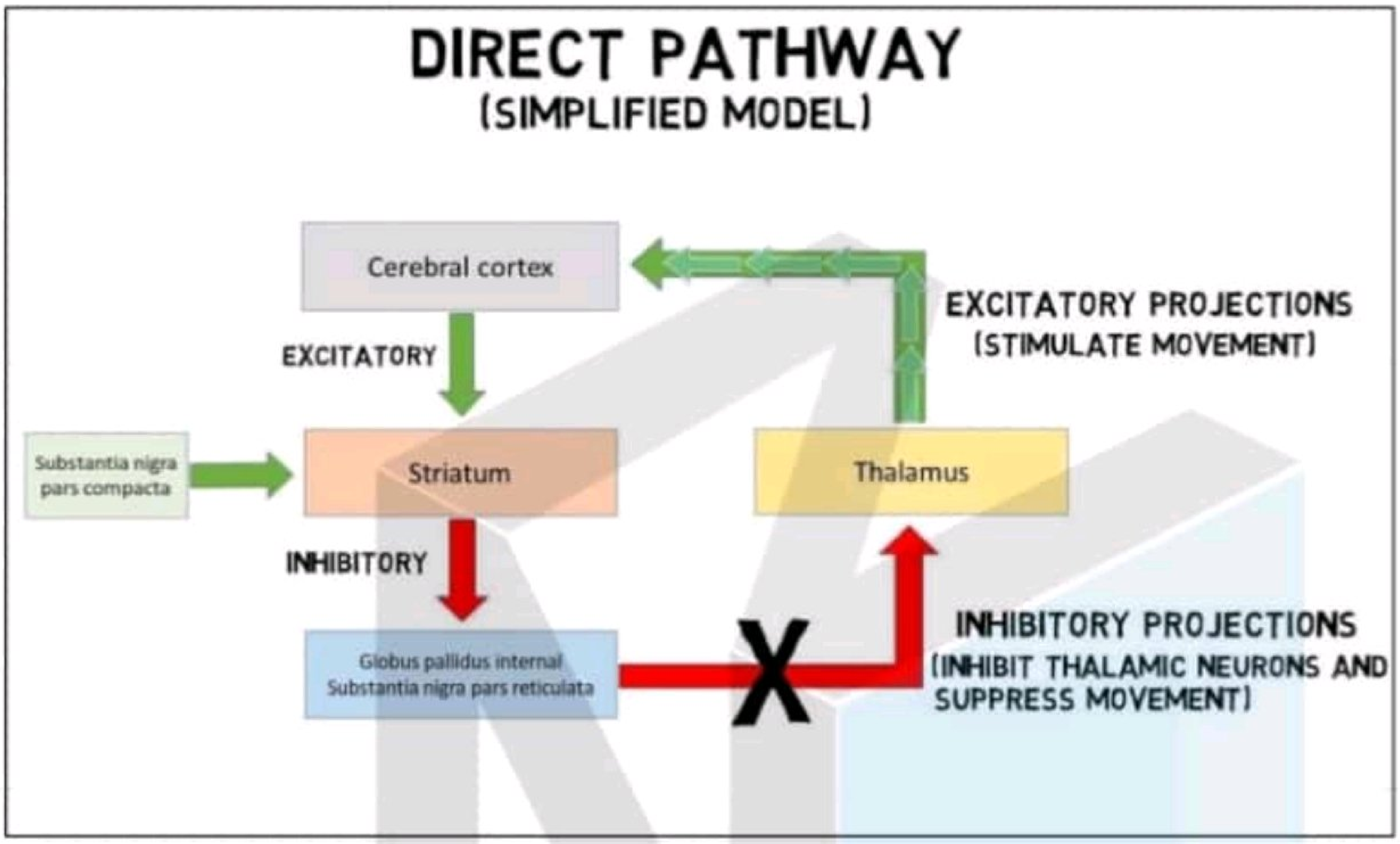
Solid lines indicate excitatory pathways, dashed lines indicate inhibitory pathways. The transmitters are indicated in the pathways, where they are known. DA, dopamine; Glu, glutamate. Acetylcholine is the transmitter produced by interneurons in the striatum. ES, external segment; IS, internal segment; PPN, pedunculopontine nuclei; SNPC, substantia nigra, pars compacta; SNPR, substantia nigra, pars reticulata. The subthalamic nucleus also projects SNPC.

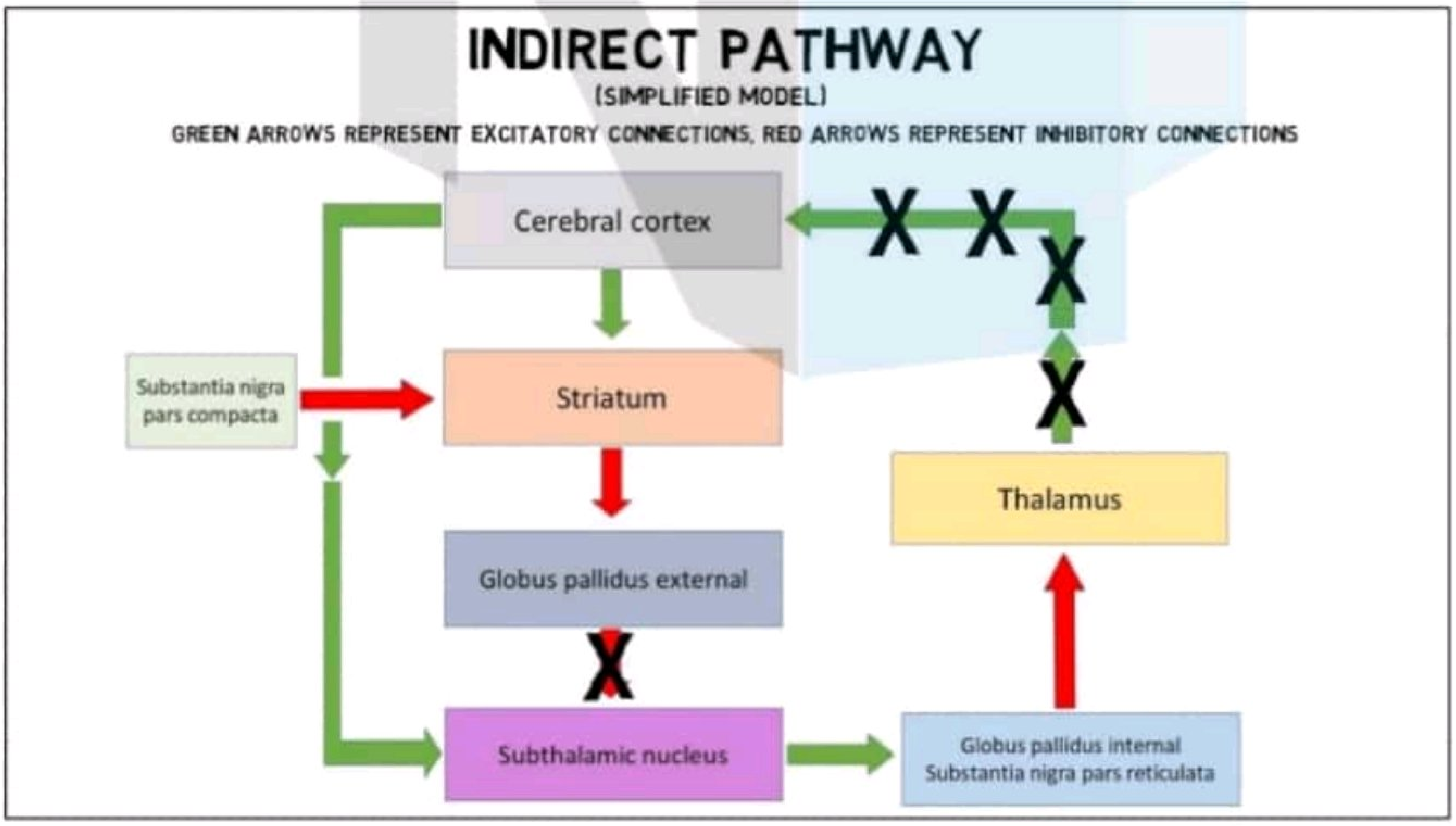


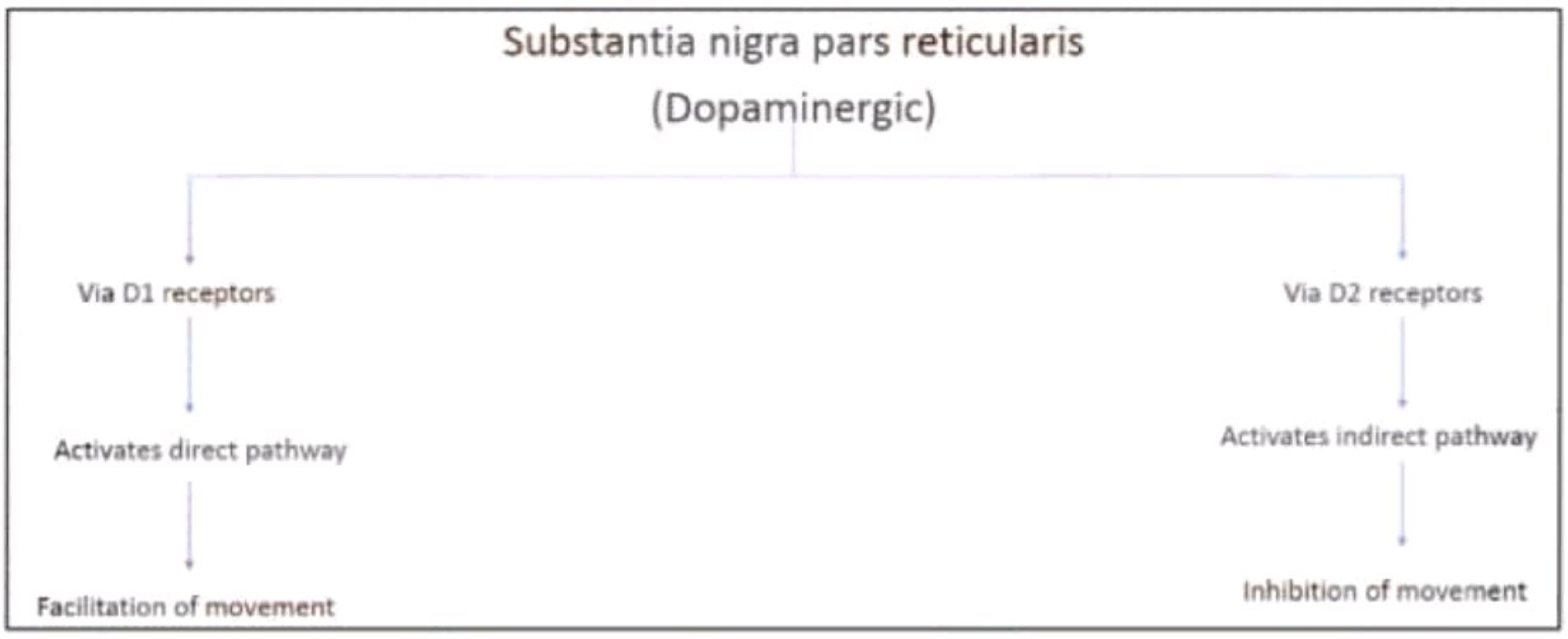
- Direct pathway→ facilitation of movement
- Indirect pathway→ inhibition of movement

- DIRECT PATHWAY (DISINHIBITION PATHWAY)
  - D1 Receptors of Stratum excite Striatum which more strongly inhibits Globus Pallidus, IS; which results in less inhibition of Thalamus by GPIS. Henceforth, the Thalamus is EXCITED.

- INDIRECT PATHWAY (DISINHIBITION PATHWAY)
    - D2 Receptors of Stratum excite Striatum which more strongly inhibits Globus Pallidus, ES; which results in less inhibition of Subthamaus by GPES. This increases the Glutamate release from Subthalamus resulting in stimulation of GPIS. GPIS overactivity increases the levels of GABA secreted to inhibit the Thalamus finally. Henceforth, the Thalamus is INHIBITED.


DIRECT PATHWAY
(SIMPLIFIED MODEL)
Cerebral cortex
EXCITATORY
Substantia nigra pars compacta
Striatum
INHIBITORY
Globus pallidus internal
Substantia nigra pars reticulata
Thalamus
EXCITATORY PROJECTIONS
(STIMULATE MOVEMENT)
INHIBITORY PROJECTIONS
(INHIBIT THALAMIC NEURONS AND SUPPRESS MOVEMENT)


INDIRECT PATHWAY
(SIMPLIFIED MODEL)
GREEN ARROWS REPRESENT EXCITATORY CONNECTIONS, RED ARROWS REPRESENT INHIBITORY CONNECTIONS
Cerebral cortex
Substantia nigra pars compacta
Striatum
Globus pallidus external
Subthalamic nucleus
Globus pallidus internal
Substantia nigra pars reticulata
Thalamus



Substantia nigra pars reticularis
(Dopaminergic)

Via D1 receptors

Activates direct pathway

Facilitation of movement

Via D2 receptors

Activates indirect pathway

Inhibition of movement

Functions of basal ganglia

- Planning and programming of movement
- Involved in processes which convert an abstract thought into a voluntary movement
- Control and co-ordinate complex patterns of movement, automatic, skilled movements and associated movements
- In close association with the cerebral cortex, timing (how rapidly a movement has to be performed) and scaling (how large a movement will be) of movements

Diseases of the basal ganglia

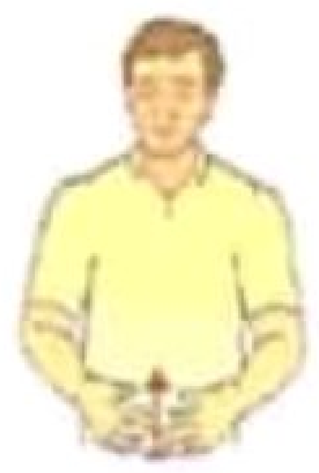
Hyperkinetic- movements are excessive and abnormal. Include

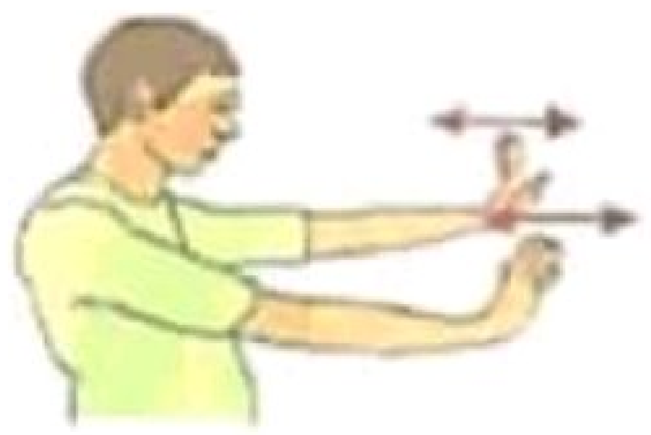
- **Chorea (**striatum esp putamen lesions)- characterized by involuntary, rapid, unco-ordinated jerking or flicking movements of hands, face and other parts of the body
- **Athetosis** (globus pallidus lesions)- characterized by spontaneous, continuous, slow, writhing movements of a hand, an arm, the neck, or the face
- **Ballism/ hemiballismus** (sub thalamic lesions)- involuntary flailing, intense and violent movements of an entire limb

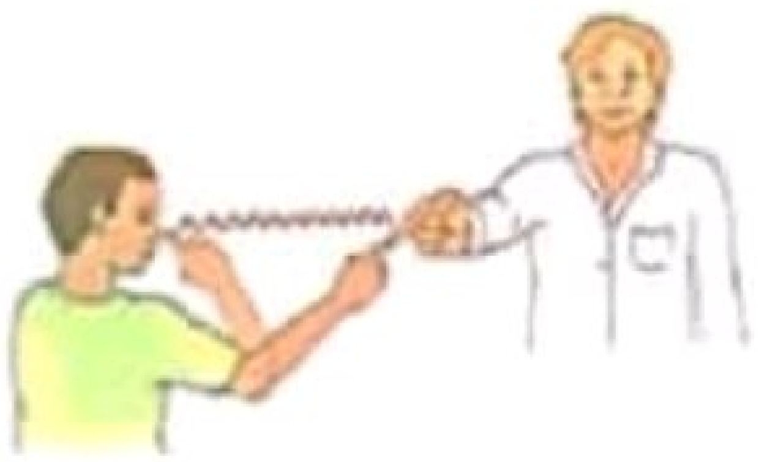
Hypokinetic abnormalities include

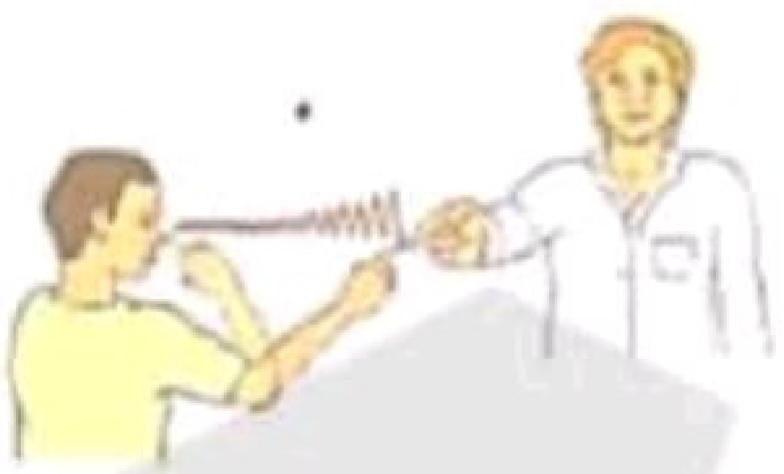
- **Bradykinesia**- slowness of movement
- **Akinesia**- difficulty in initiating movement and decreased spontaneous movement

TREMORS

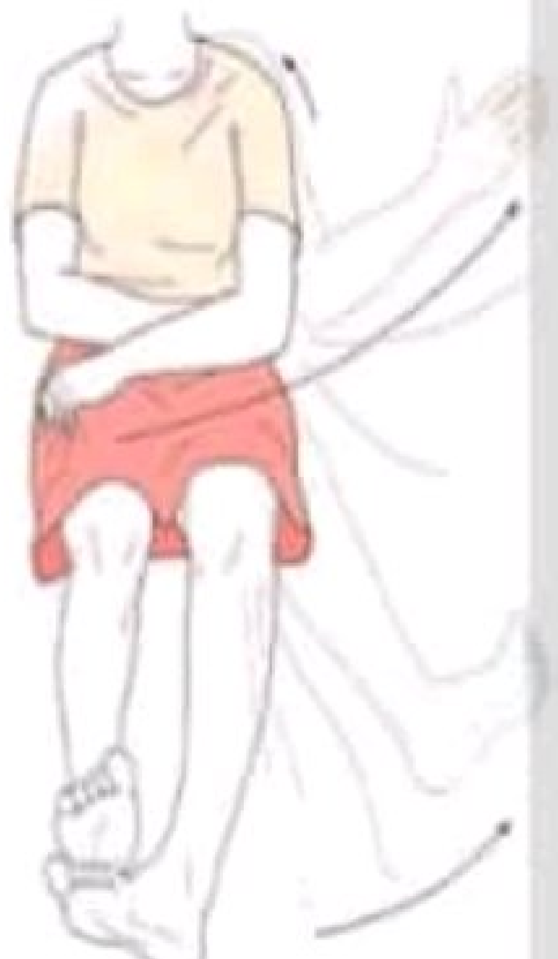

RESTING

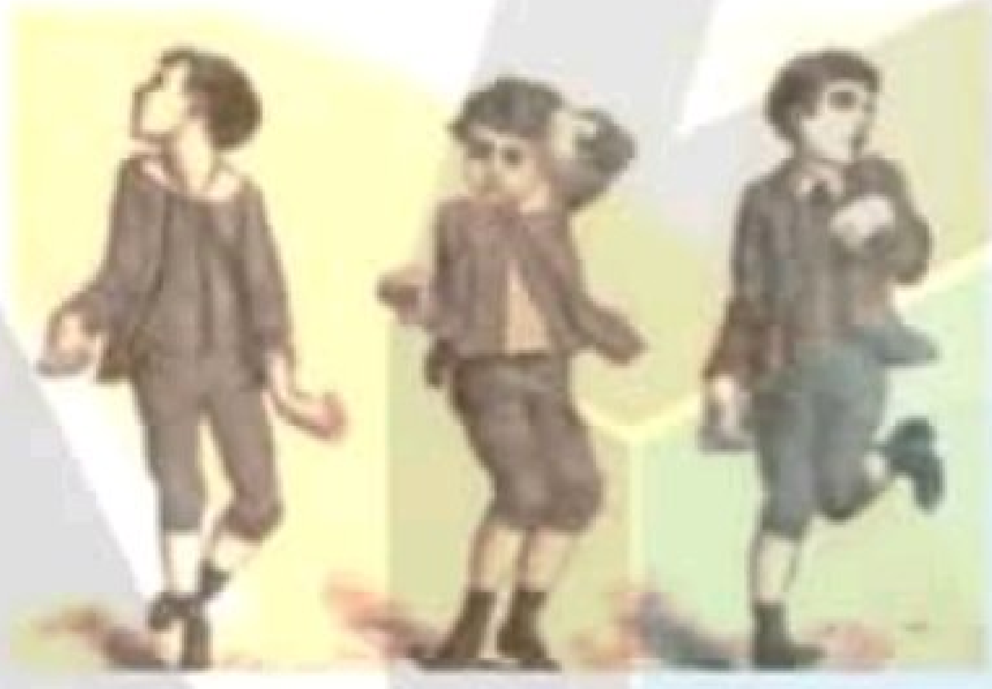

FLAPPING

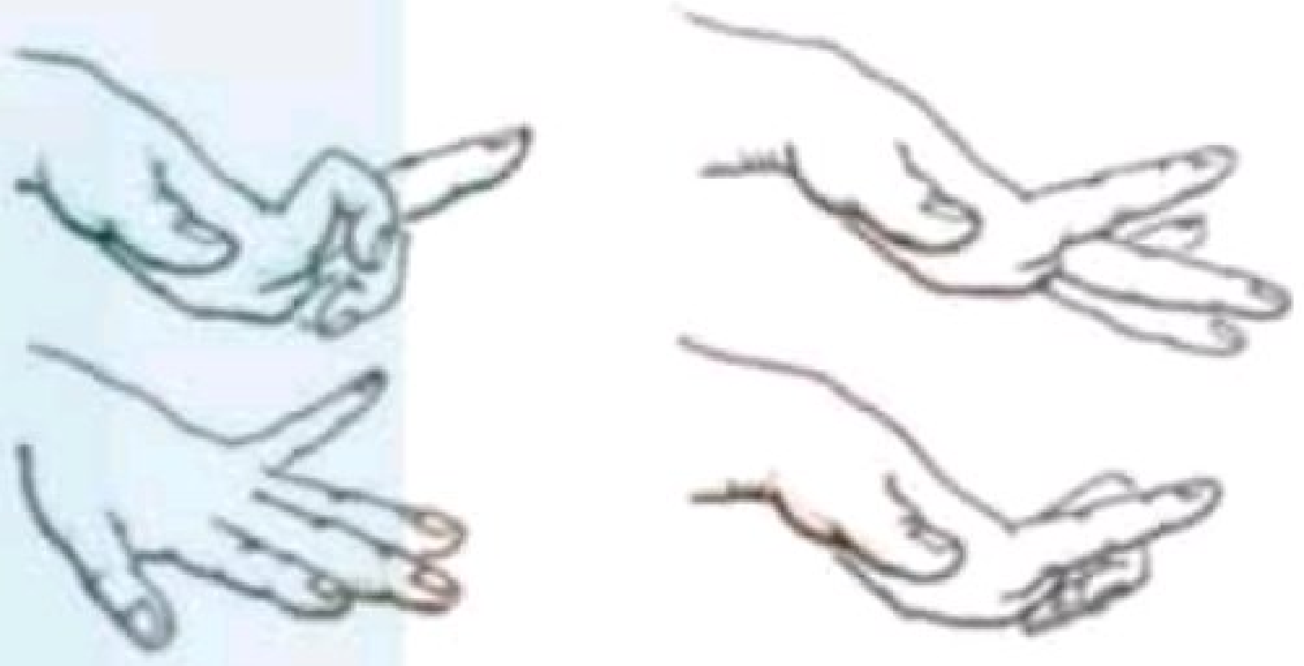

ESSENTIAL


INTENTIONAL

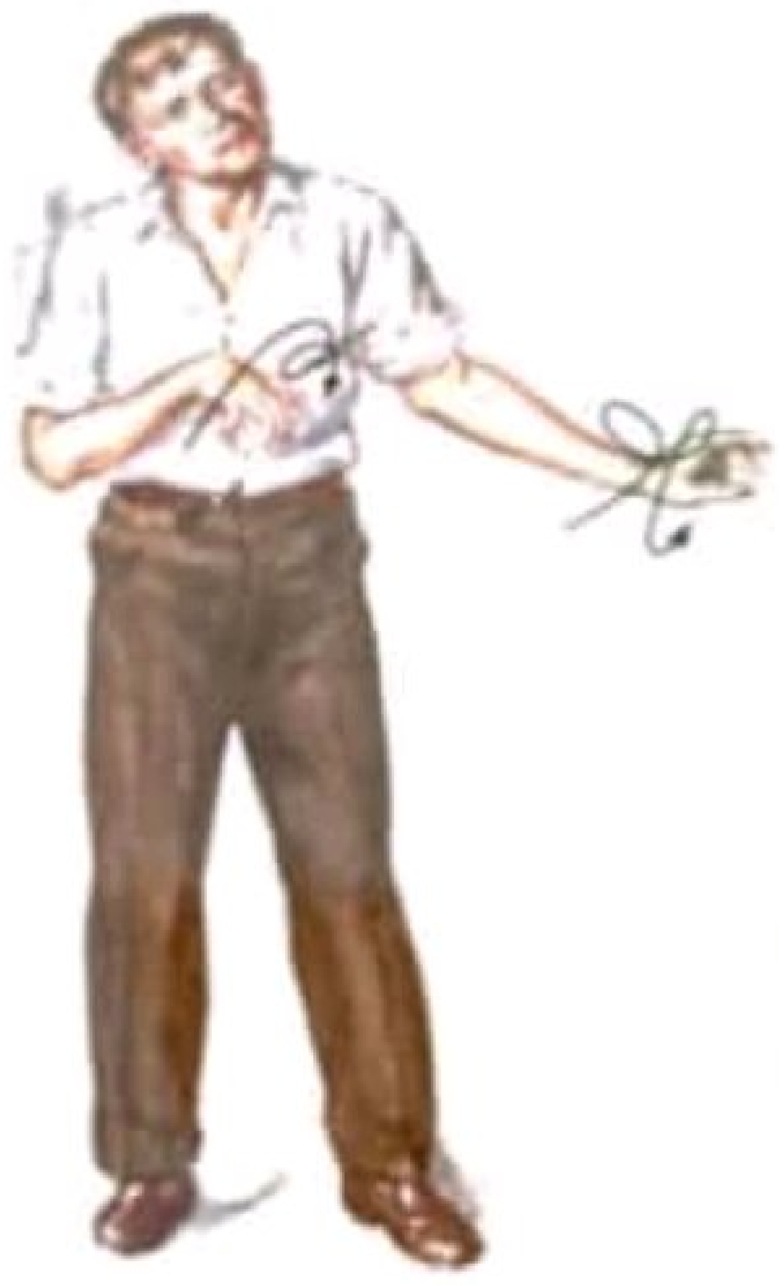
MOVEMENT DISORDER

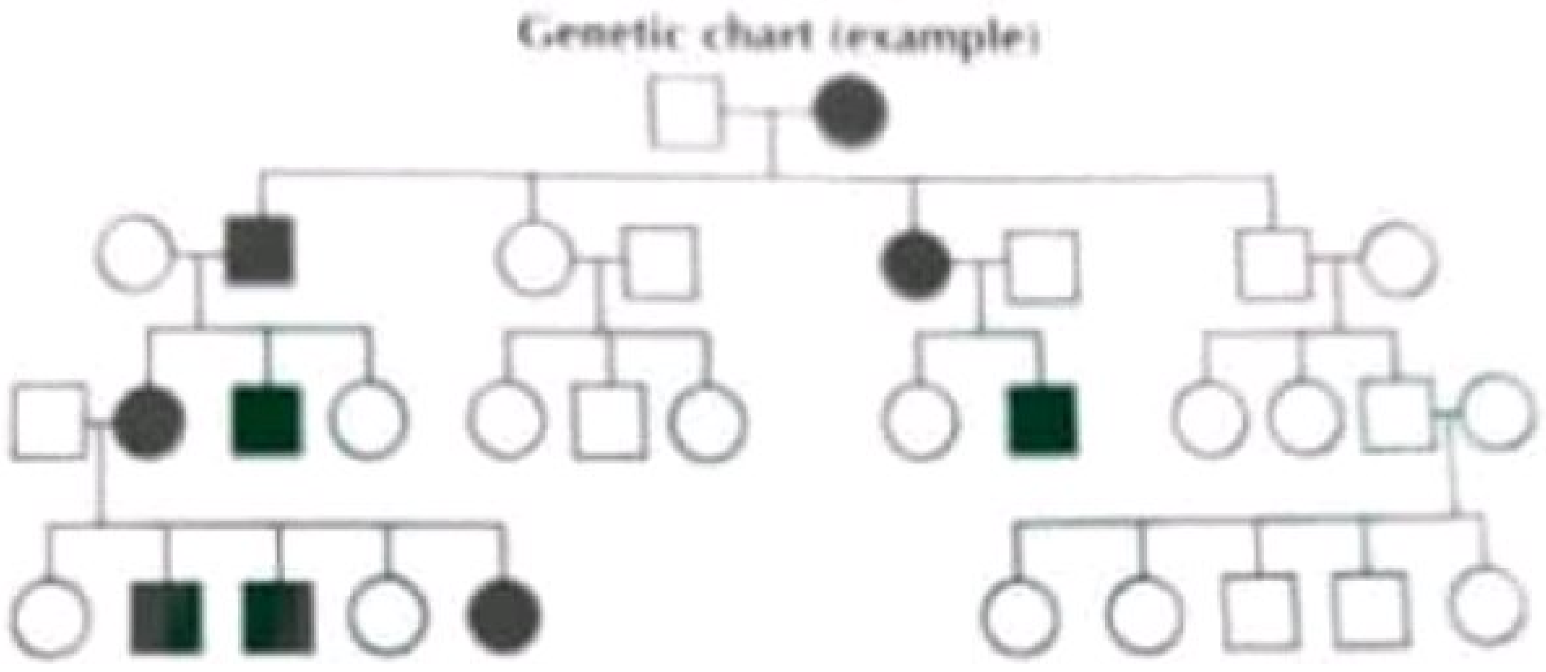

HEMIBALLISMUS


CHOREA


ATHETOSIS

HUNTINGTON CHOREA


CHOREO
ATHETOID
MOVEMENTS

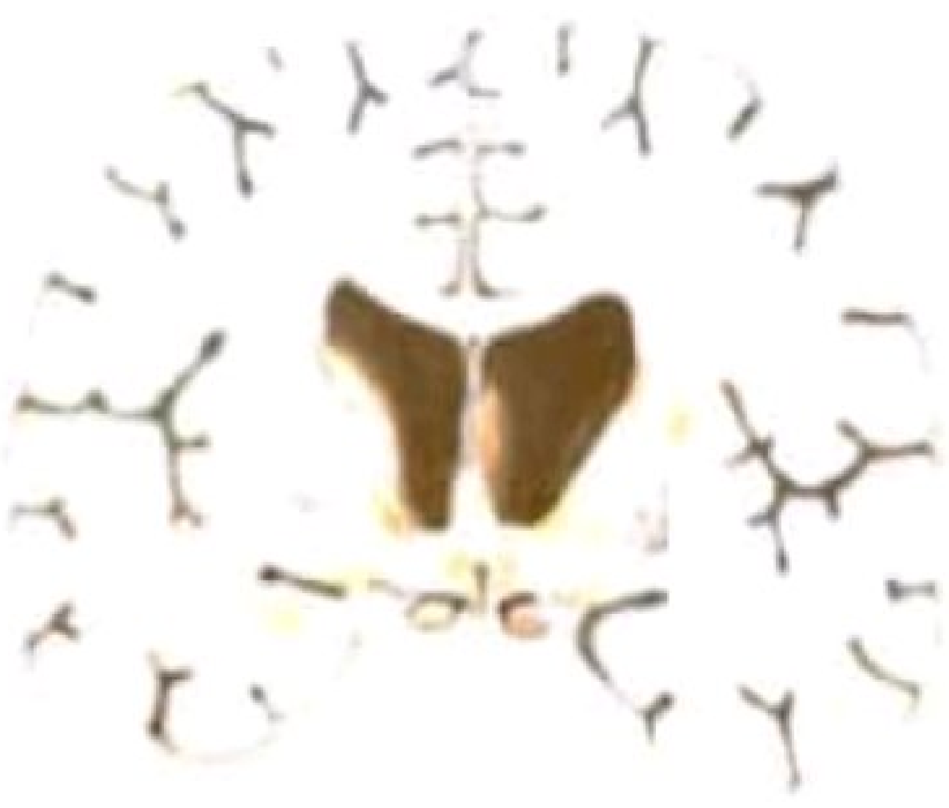


AD INHERITANCE

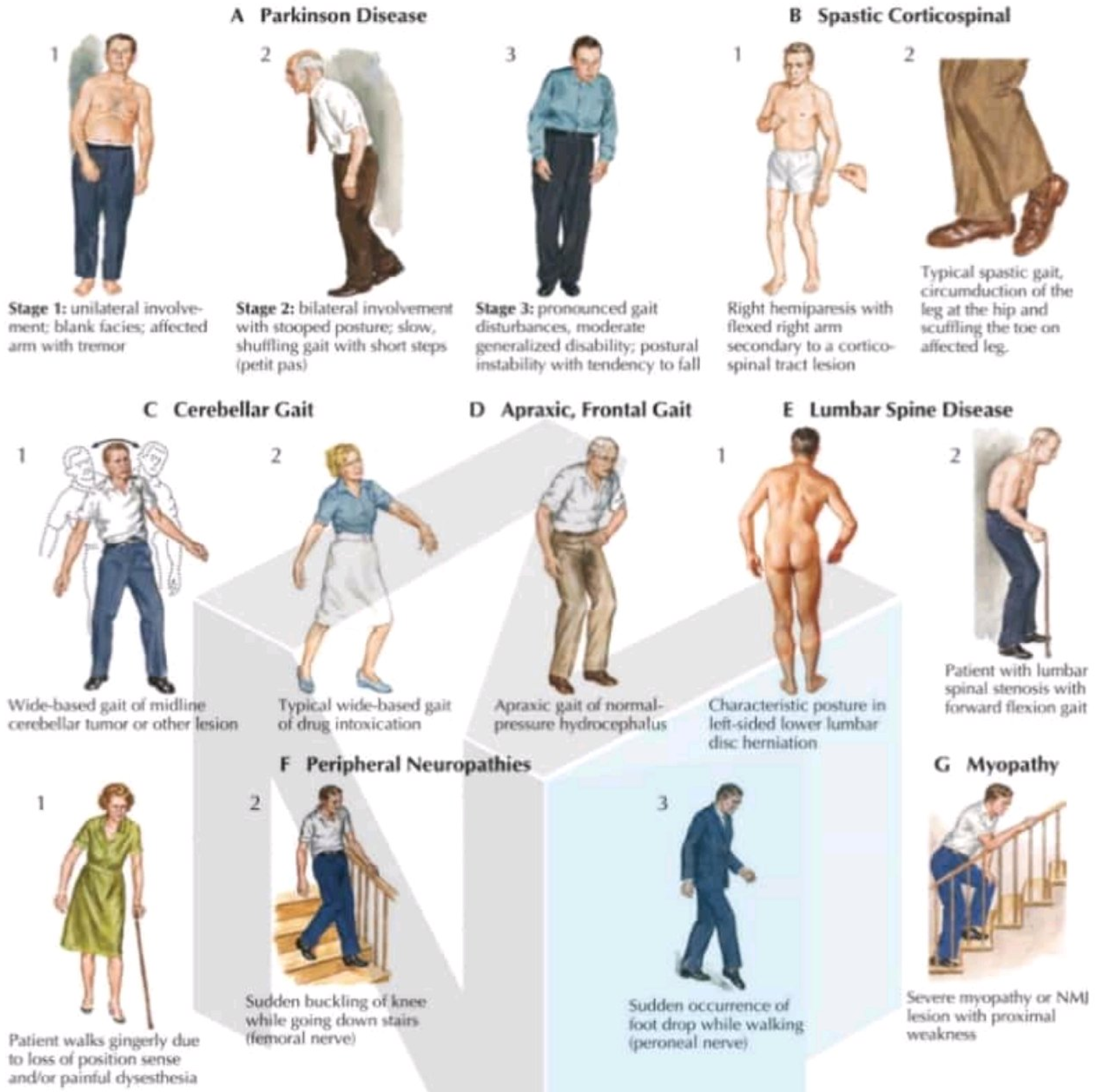
ANTICIPATION

DEMENTIA

ATROPHY IN CAUDATE NUCLEUS
INTRASTRIATAL LOSS OF ACH,GABA ACTIVITY
INCREASED DOPAMERGIC ACTIVITY



Gait disorders



A Parkinson Disease

1 **Stage 1:** unilateral involvement; blank facies; affected arm with tremor

2 **Stage 2:** bilateral involvement with stooped posture; slow, shuffling gait with short steps (petit pas)

3 **Stage 3:** pronounced gait disturbances, moderate generalized disability; postural instability with tendency to fall

B Spastic Corticospinal

1 Right hemiparesis with flexed right arm secondary to a corticospinal tract lesion

2 Typical spastic gait, circumduction of the leg at the hip and scuffling the toe on affected leg.

C Cerebellar Gait

1 Wide-based gait of midline cerebellar tumor or other lesion

2 Typical wide-based gait of drug intoxication

D Apraxic, Frontal Gait

Apraxic gait of normal-pressure hydrocephalus

E Lumbar Spine Disease

1 Characteristic posture in left-sided lower lumbar disc herniation

2 Patient with lumbar spinal stenosis with forward flexion gait

F Peripheral Neuropathies

1 Patient walks gingerly due to loss of position sense and/or painful dysesthesia

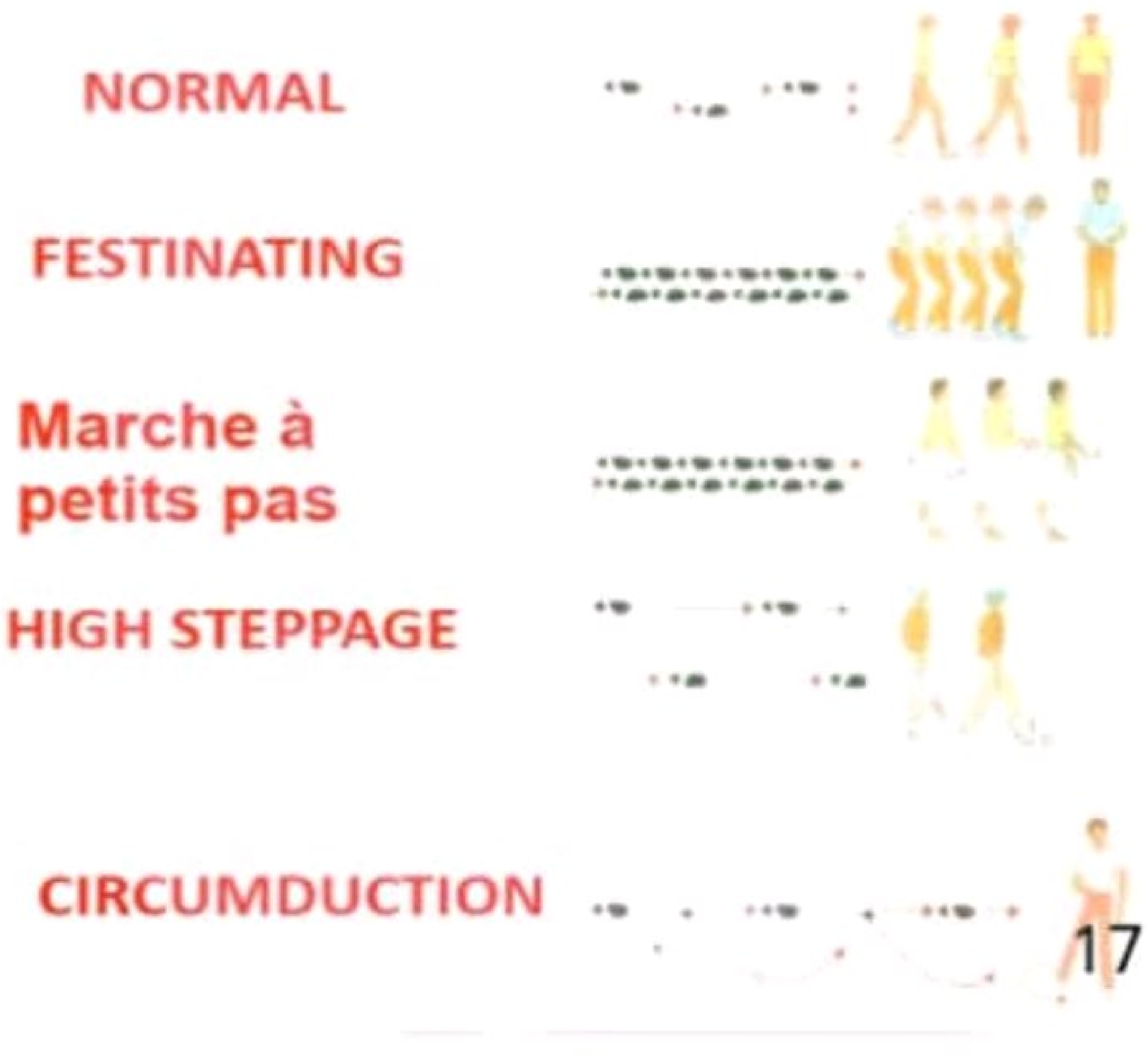
2 Sudden buckling of knee while going down stairs (femoral nerve)

3 Sudden occurrence of foot drop while walking (peroneal nerve)

G Myopathy

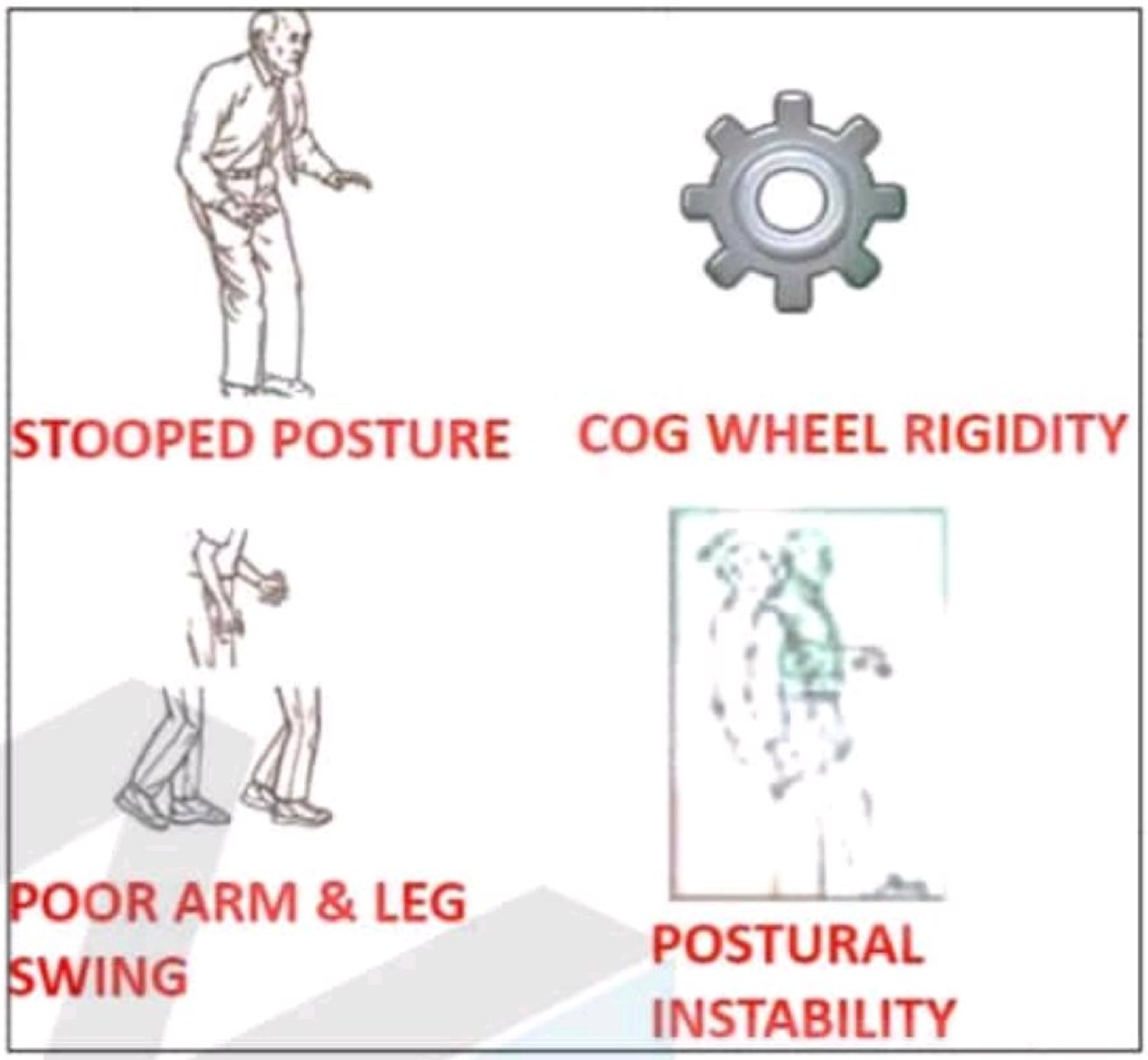
Severe myopathy or NMJ lesion with proximal weakness

GAIT DISORDERS



PARKINSON'S DISEASE

- Described by James Parkinson in 1817
- Also k/a paralysis agitans
- Has both hypokinetic and hyperkinetic features
- Hypokinetic features- bradykinesia (difficulty in initiating movement) and akinesia (absence of motor activity)
- Hyperkinetic features- tremor at rest (disappears with activity), pill rolling movements, cogwheel rigidity, lead pipe rigidity



Features Suggesting an Atypical or Secondary Cause of Parkinsonism

HISTORY	ALTERNATIVE DIAGNOSIS
Early speech and gait impairment (Lack of tremor, lack of motor asymmetry) OR poor response to L-dopa	Atypical parkinsonism
Exposure to neuroleptics	Drug-induced parkinsonism
Onset prior to age 40	Genetic form of PD
Liver disease	Wilson's disease
Early hallucinations and dementia with later development of PD features	Dementia with Lewy bodies
Impaired down gaze	PSP

CLINICAL EXAMINATION	ALTERNATIVE DIAGNOSIS
Dementia as first or early feature	Dementia with Lewy bodies
Prominent orthostatic hypotension	MSA-p
Prominent cerebellar signs	MSA-c
Slow saccades with impaired down gaze	PSP
High-frequency (6–10 Hz) symmetric postural tremor	Essential tremor

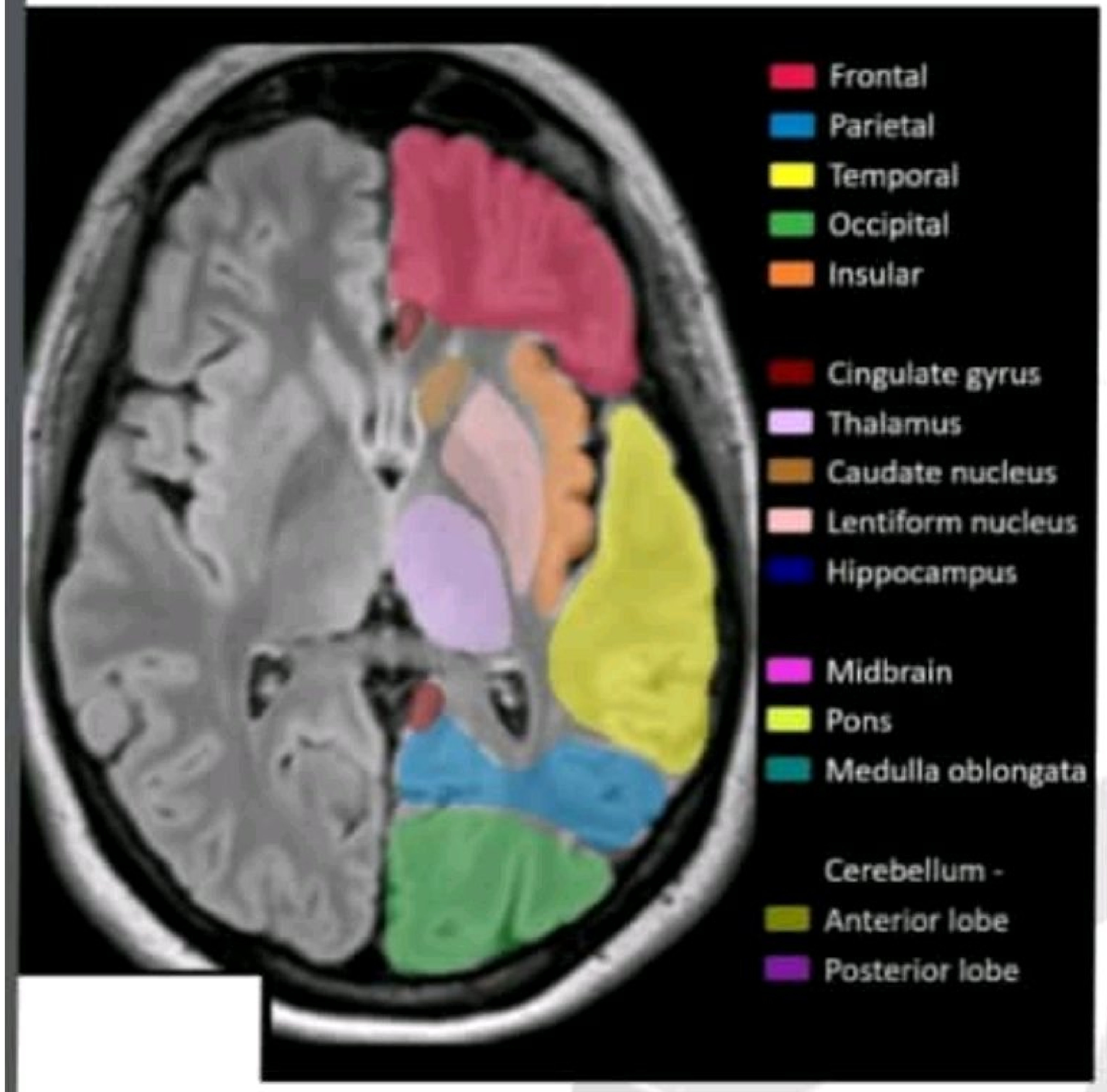
Genetic form of PD: LRRK2 Gene

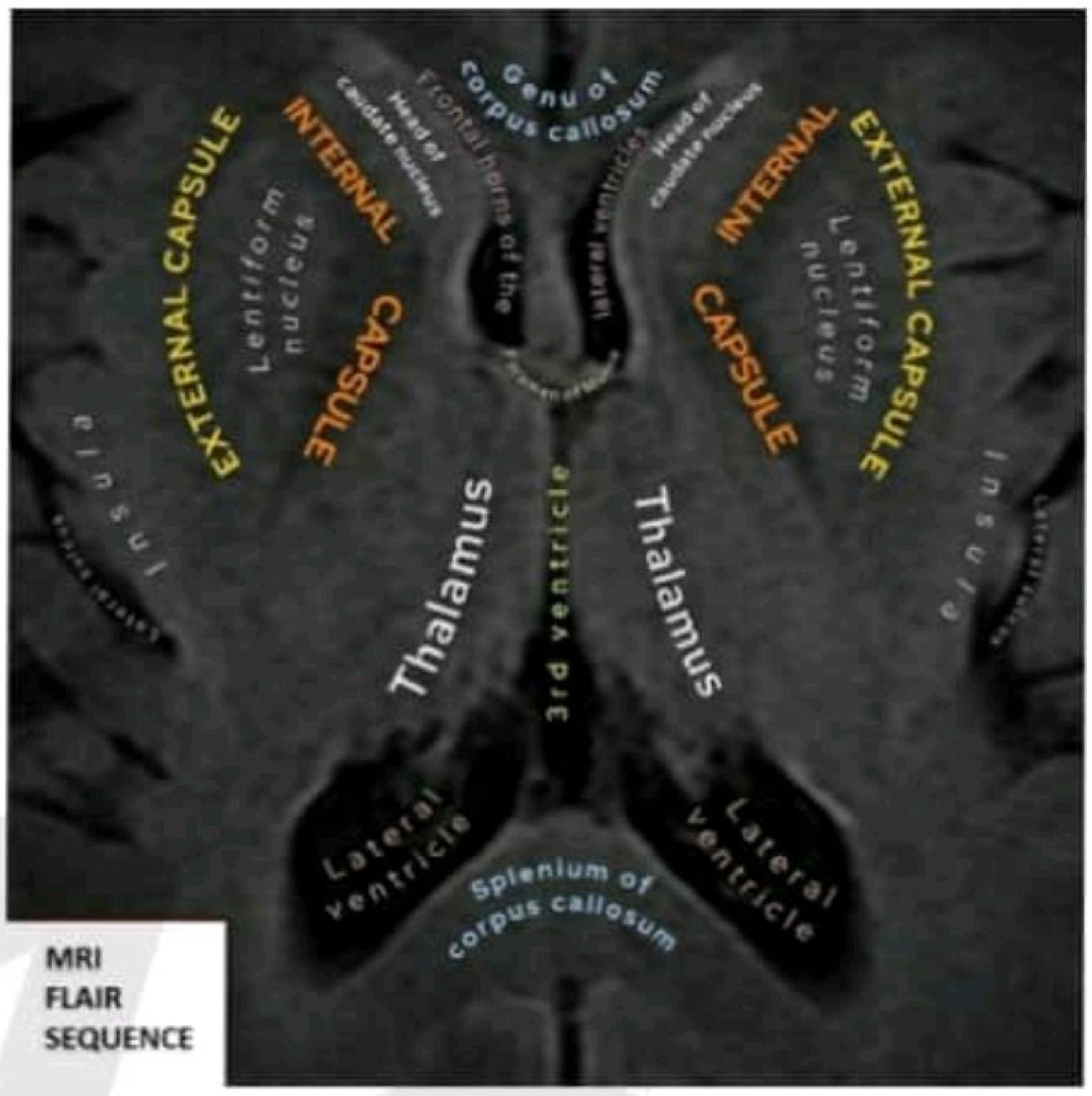
PSP: Progressive Supranuclear Palsy

MSA: Multiple System Atrophy

Alien-Limb phenomena→ Cortico-basilar degeneration

RADIOLOGY


🟥 Frontal
🟦 Parietal
🟨 Temporal
🟩 Occipital
🟧 Insular
Cingulate gyrus
Thalamus
Caudate nucleus
Lentiform nucleus
Hippocampus
Midbrain
Pons
Medulla oblongata
Cerebellum -
Anterior lobe
Posterior lobe


Genu of corpus callosum
Head of caudate nucleus
Frontal horns of the lateral ventricles
INTERNAL CAPSULE
EXTERNAL CAPSULE
Lentiform nucleus
Insula
Thalamus
3rd ventricle
Thalamus
Lateral ventricle
Splenium of corpus callosum
Lateral ventricle

MRI
FLAIR
SEQUENCE

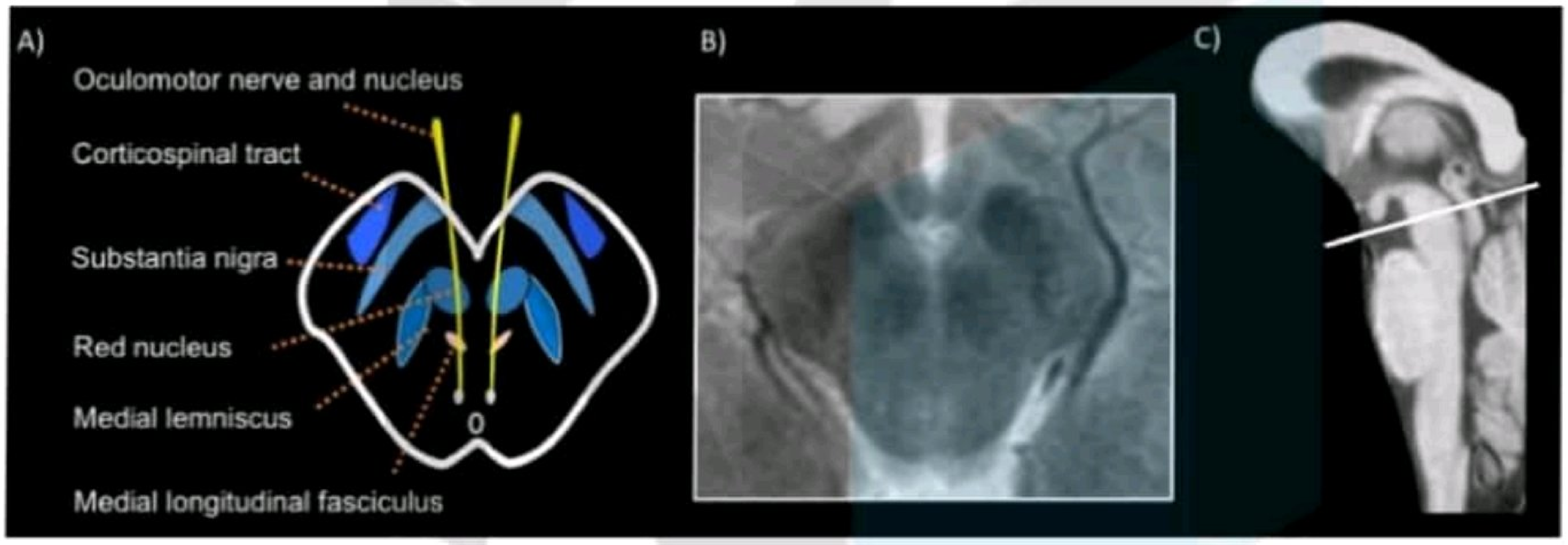
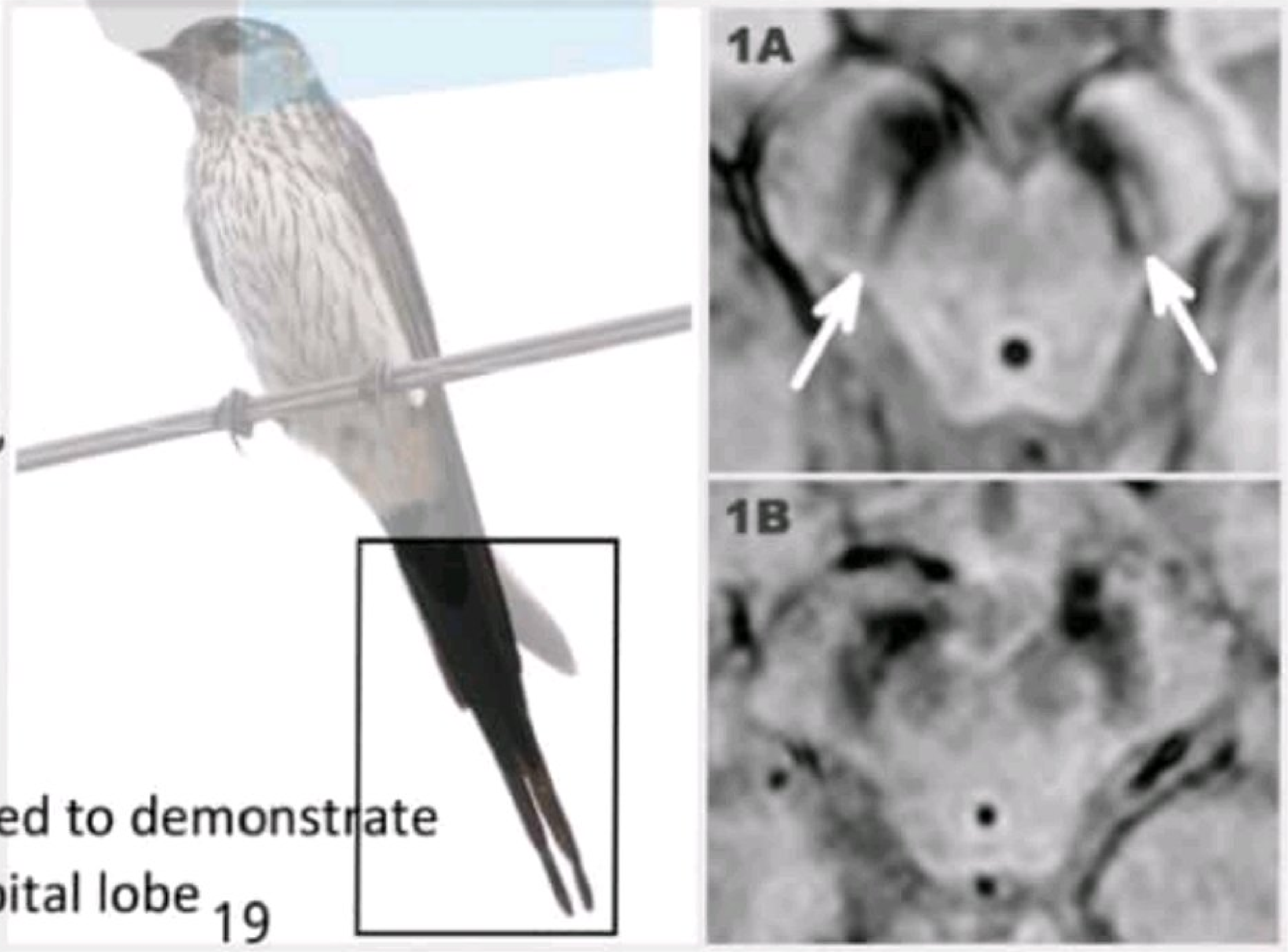

A)
Oculomotor nerve and nucleus
Corticospinal tract
Substantia nigra
Red nucleus
Medial lemniscus
Medial longitudinal fasciculus
0
B)
C)

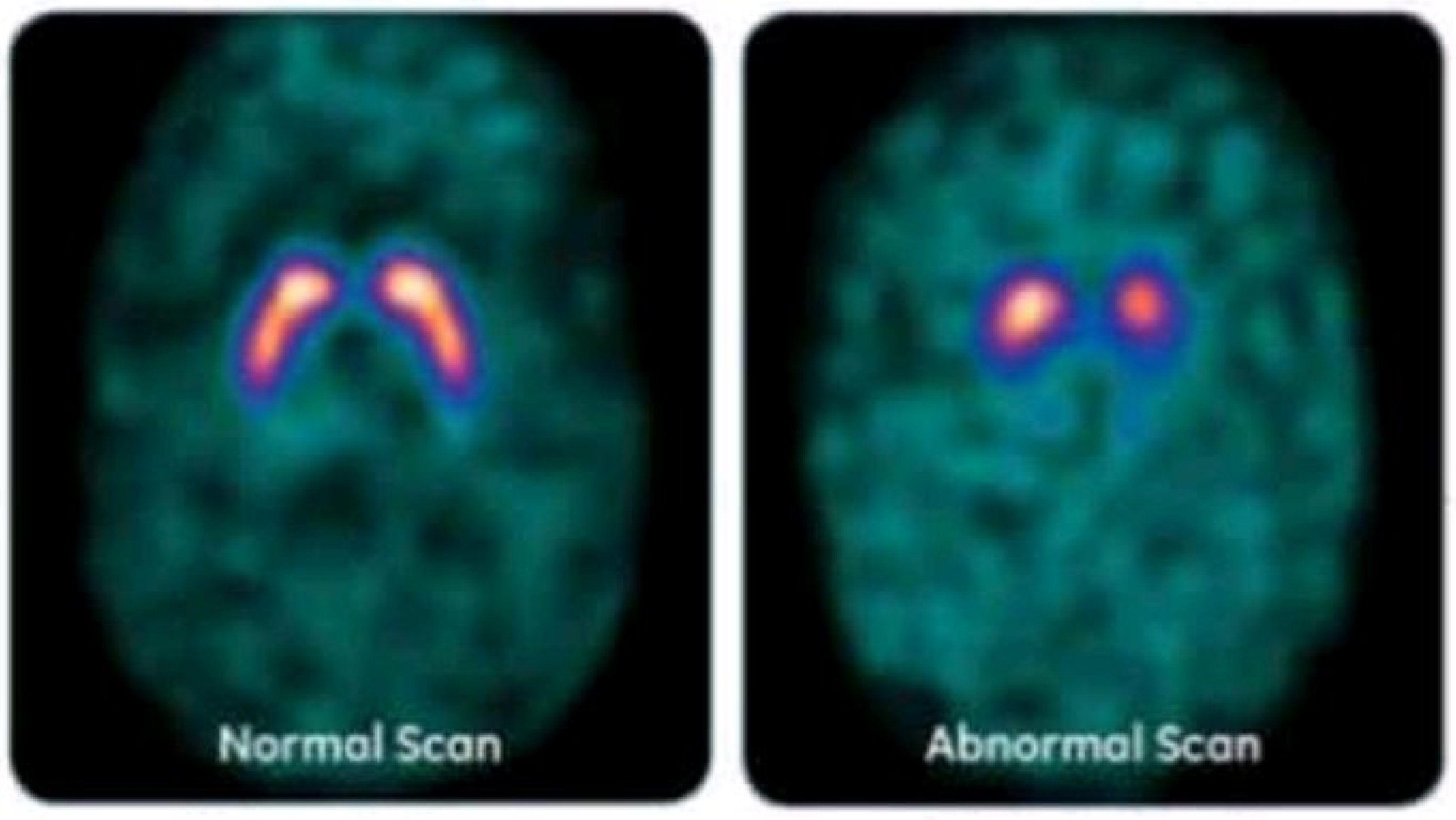
Image 1A: NORMAL
Swallow Tail Sign due to
NIGROSOME 1

Image 1B:
Loss of Swallow Tail appearance,
Seen in
1) Parkinsons's Ds
2) Lewy Body Dementia



To differentiate LBD, you will need to demonstrate
Decreased Blood supply to Occipital lobe
On PET Scan

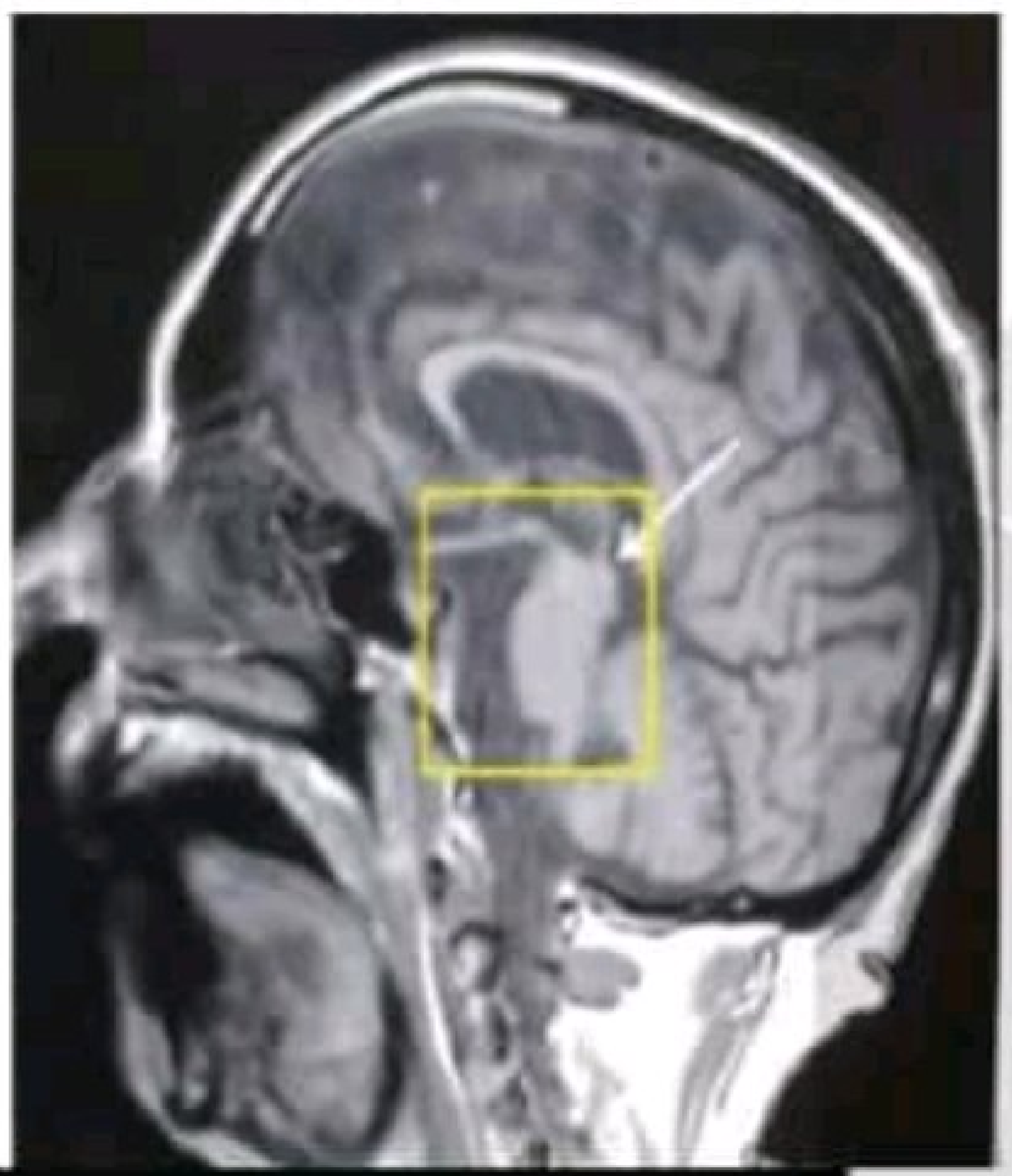
DaT Scan→ IOFLUPANE contrast (Test done in patients of Essential tremors)

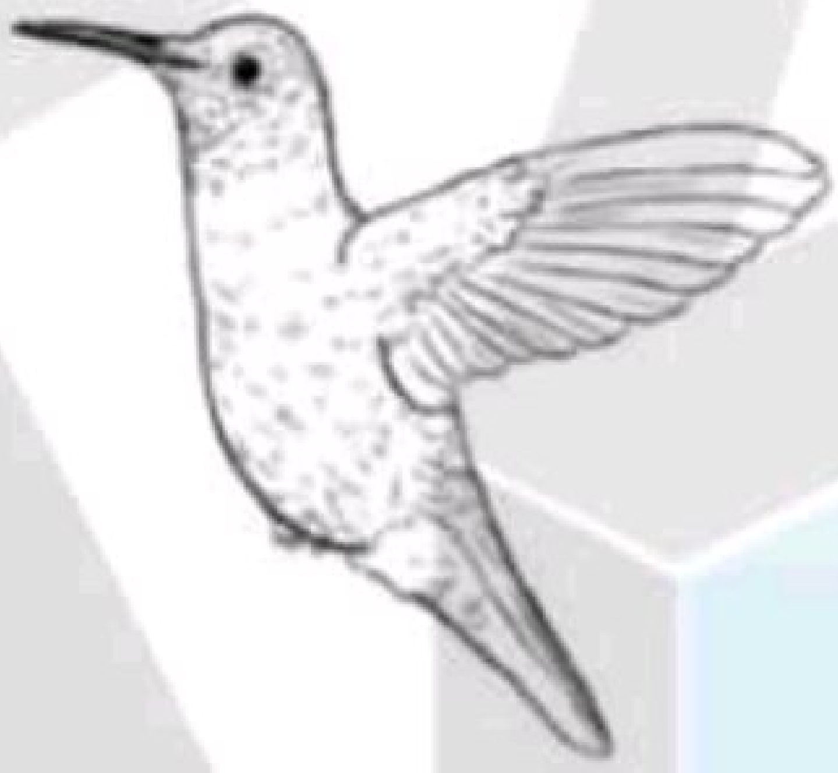


"Comma"-shaped
Possible essential tremor

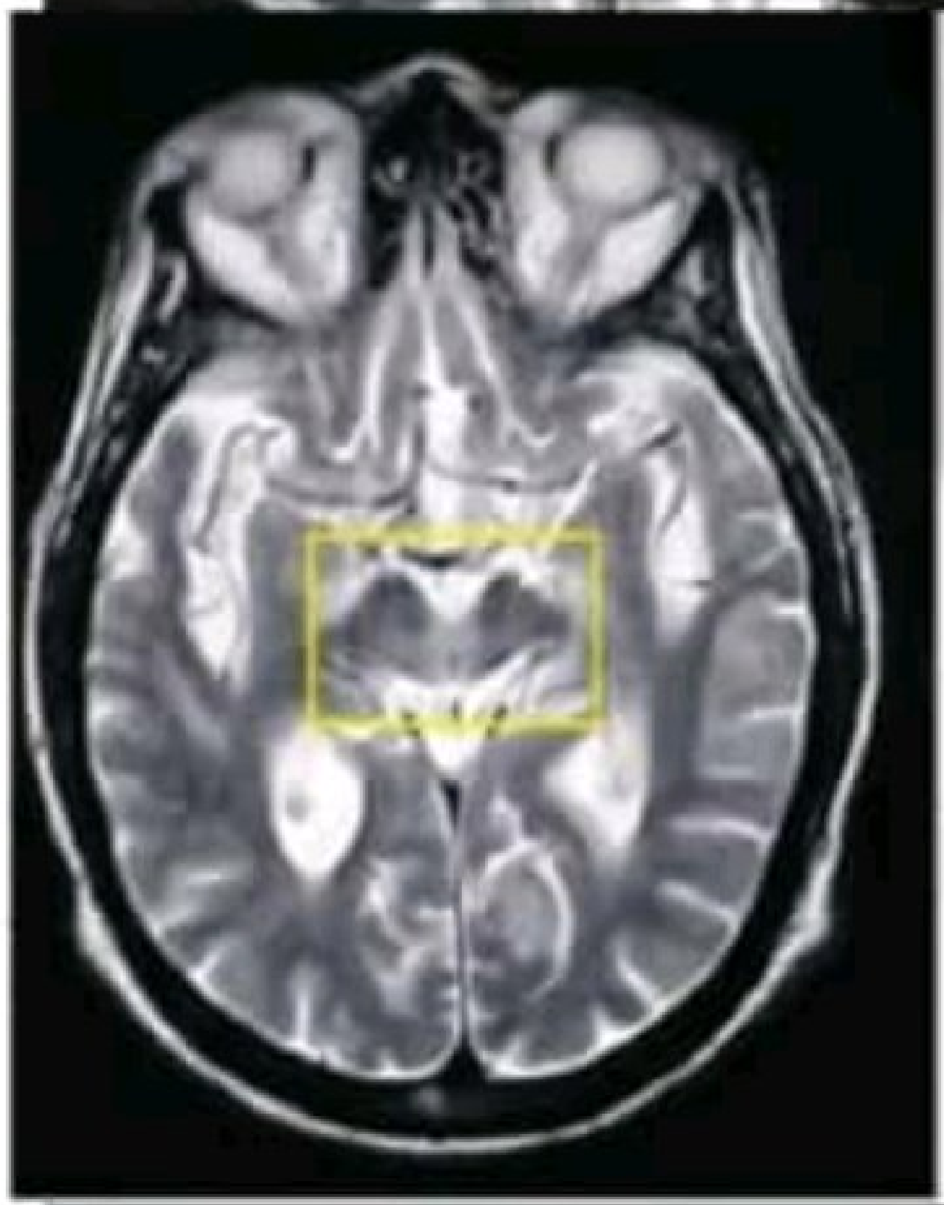
"Period"-shaped
Possible parkinsonian syndrome

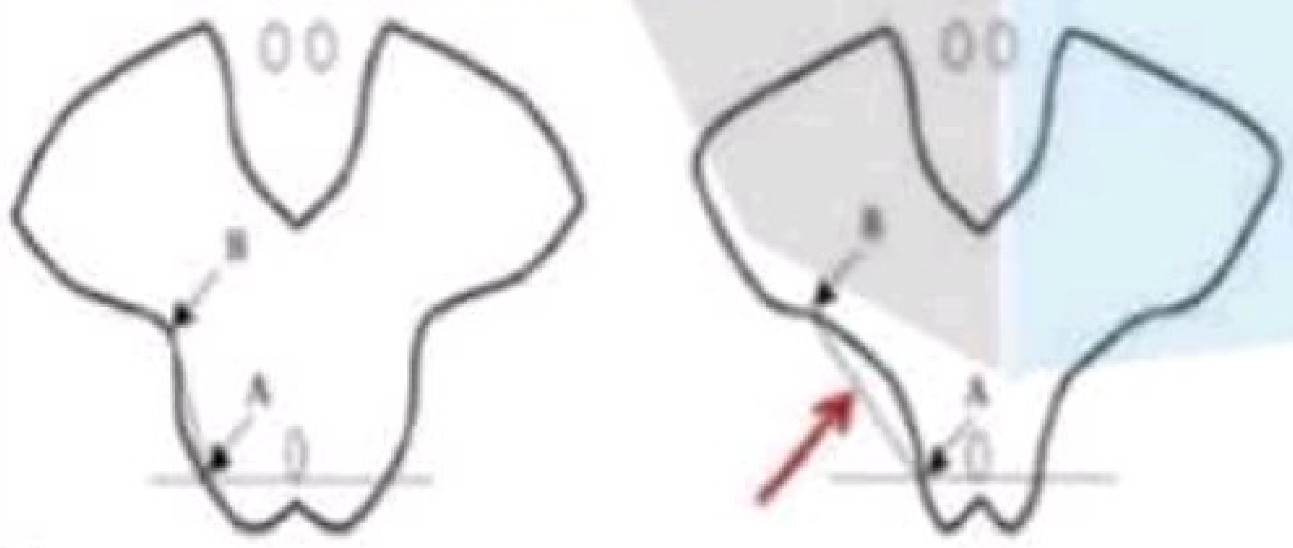
SIGNS FOR PROGRESSIVE SUPRANUCLEAR PALSY (PSP)



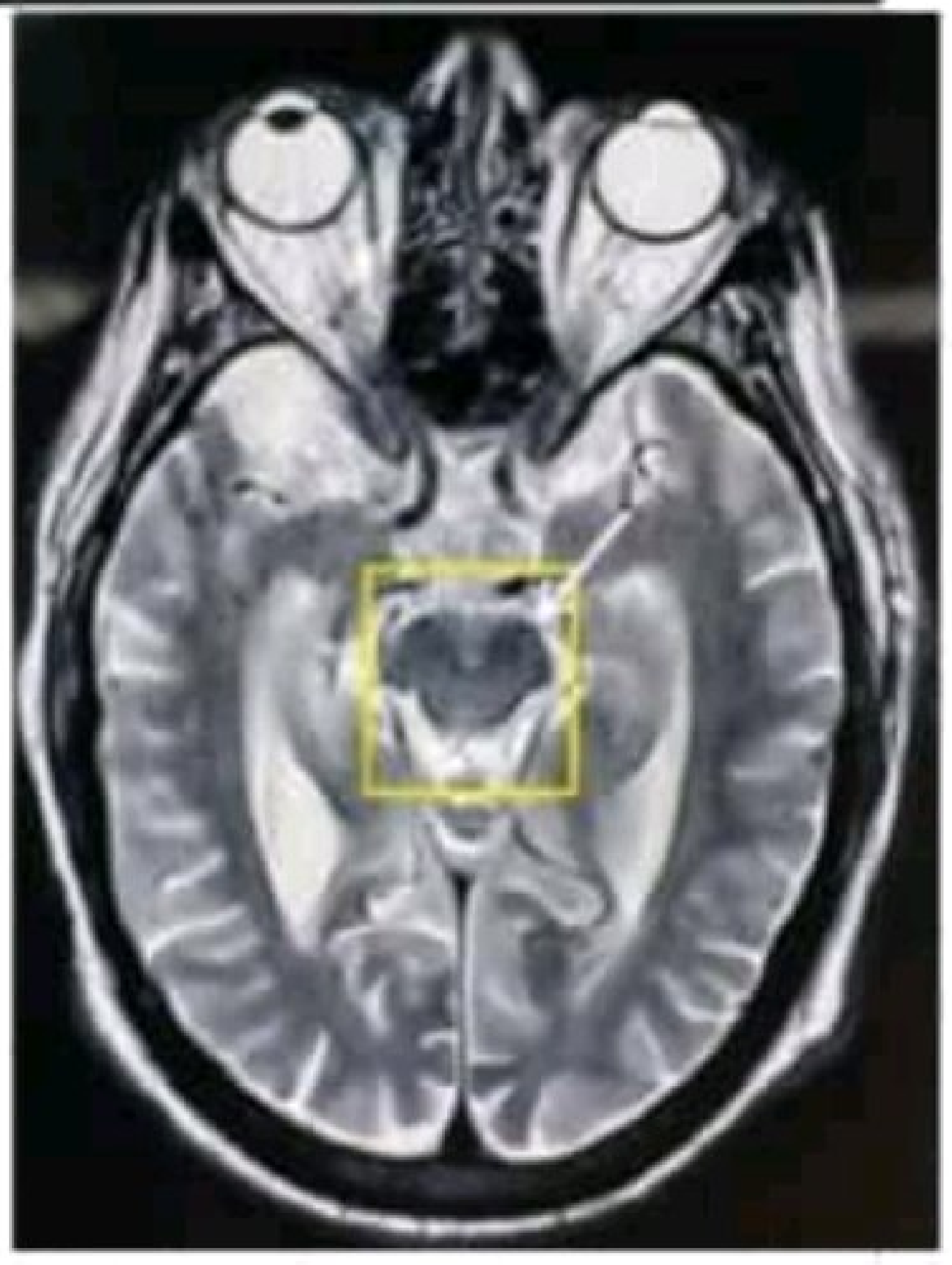


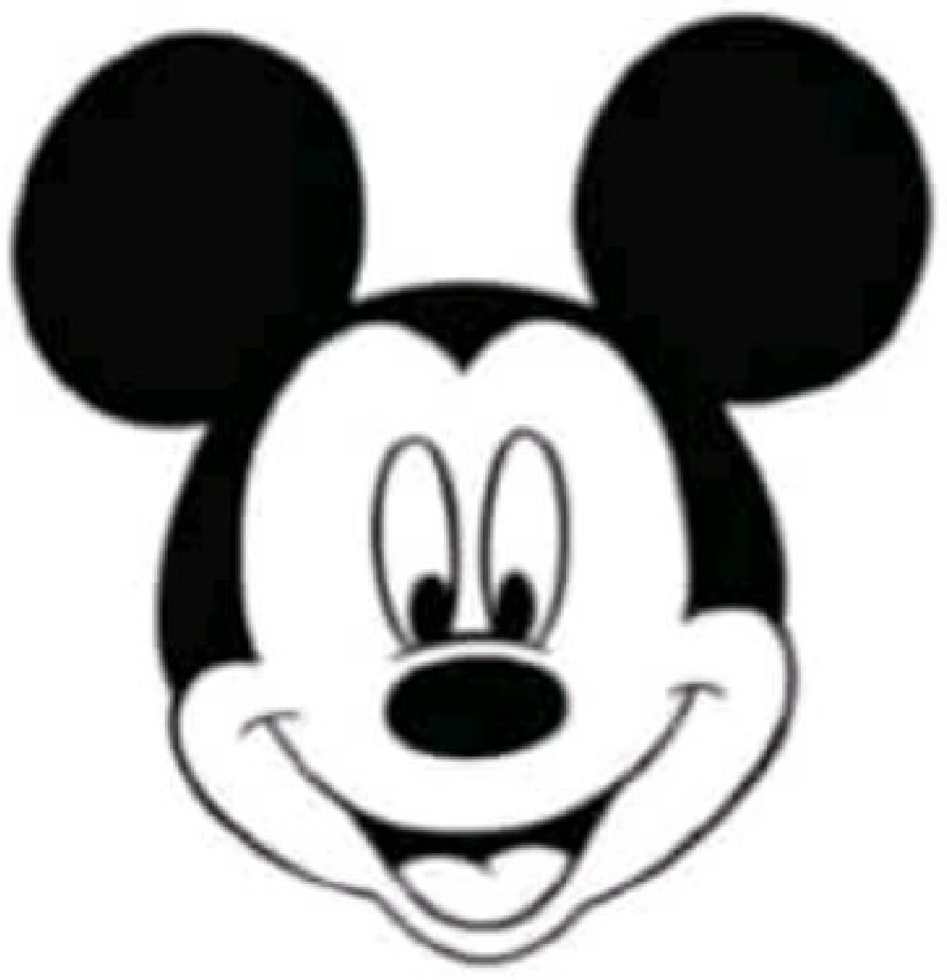
1) HUMMING BIRD APPEARANCE IN MIDBRAIN





2) MORNING GLORY SIGN

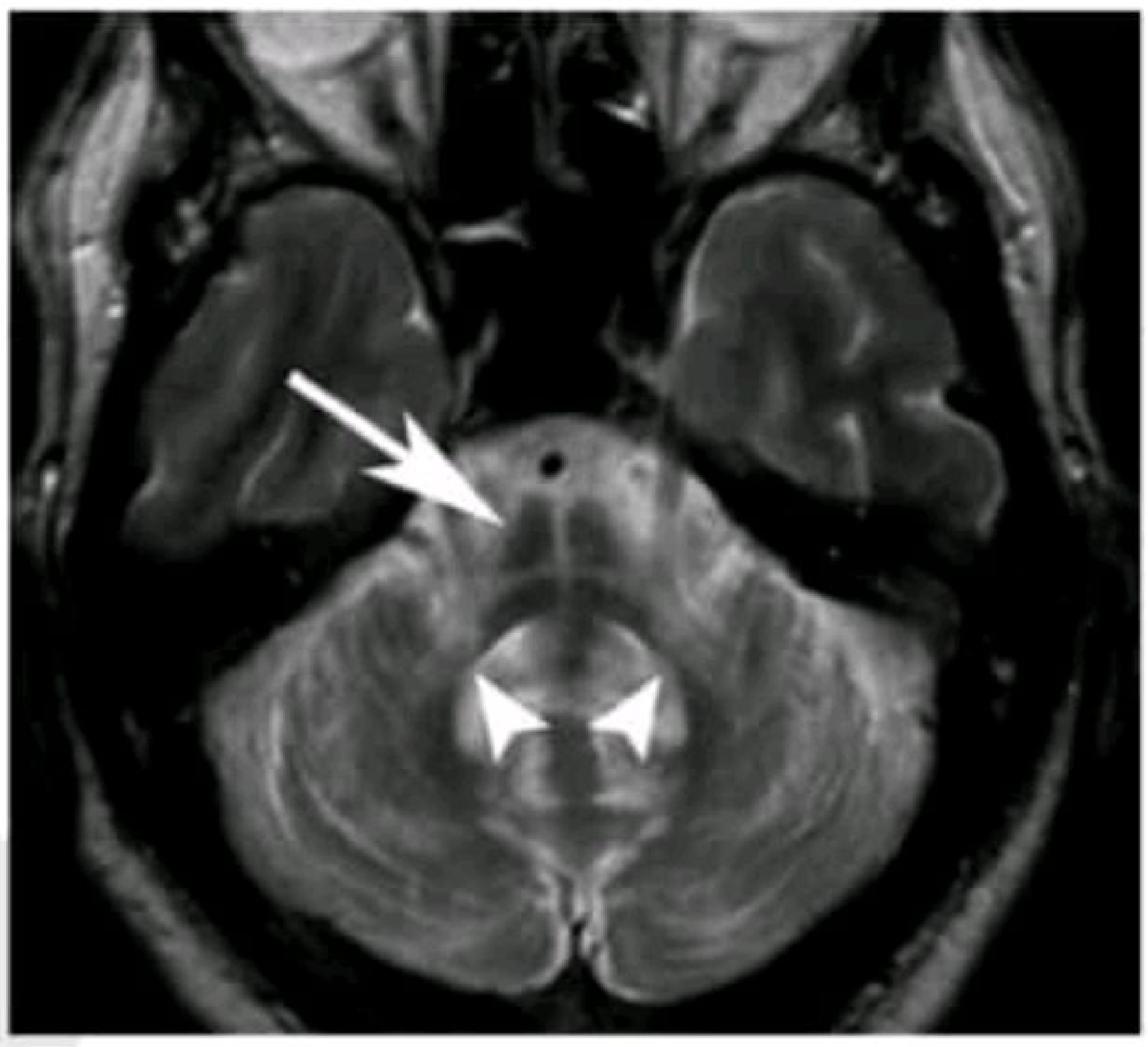




3) MICKEY MOUSE SIGN

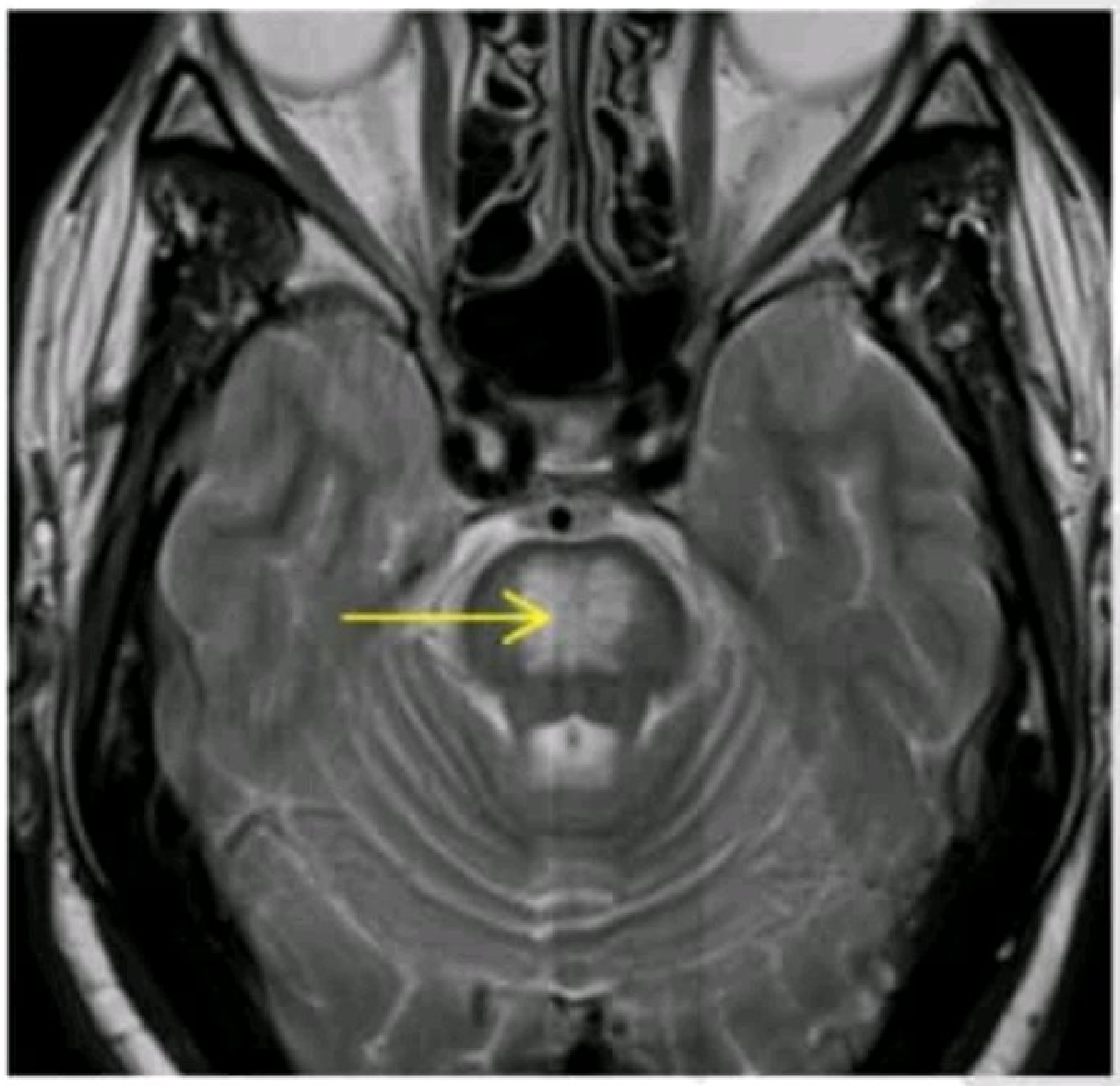
MULTIPLE SYSTEMIC ATROPHY (MSA)

MSA-C a/k/a Olivopontocerebellar degeneration (OPCD)



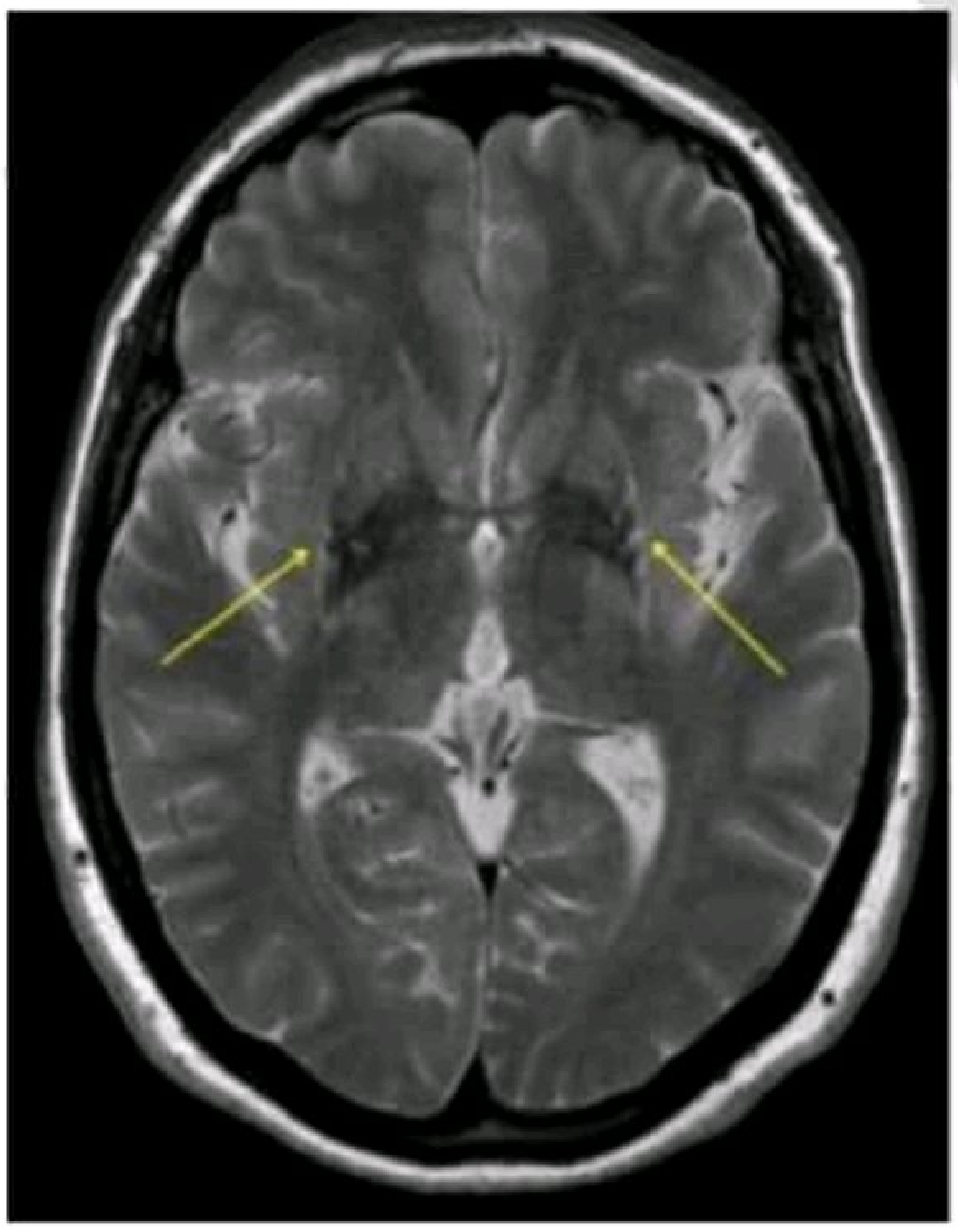
Cerebellar Atrophy: Arrowhead

HOT CROSS BUN PONS: Arrow



PONS are centrally opaque with sparing of periphery and corticospinal and pyramidal fibres

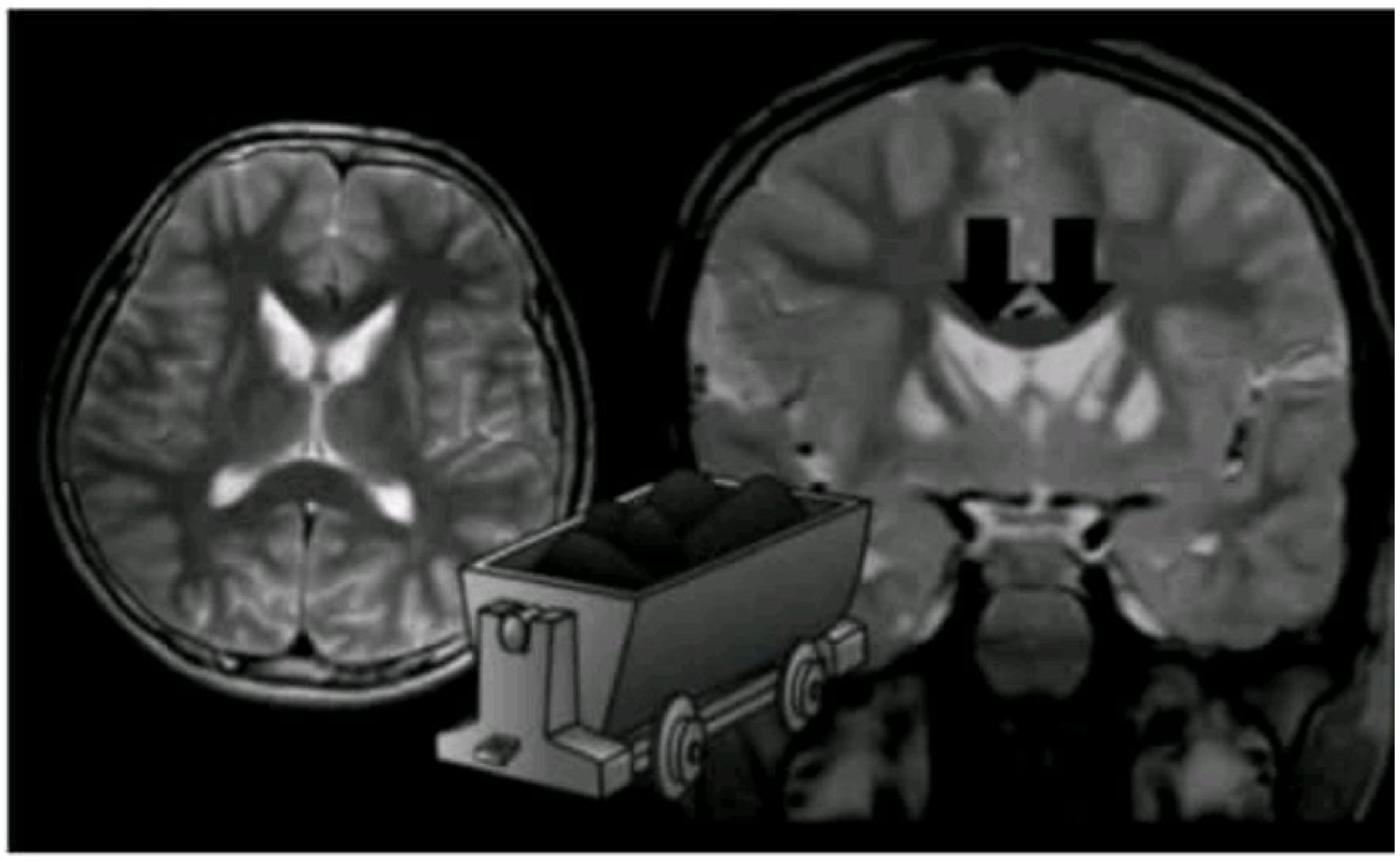
Seen in **Central Pons Myelinolysis (CPM)**

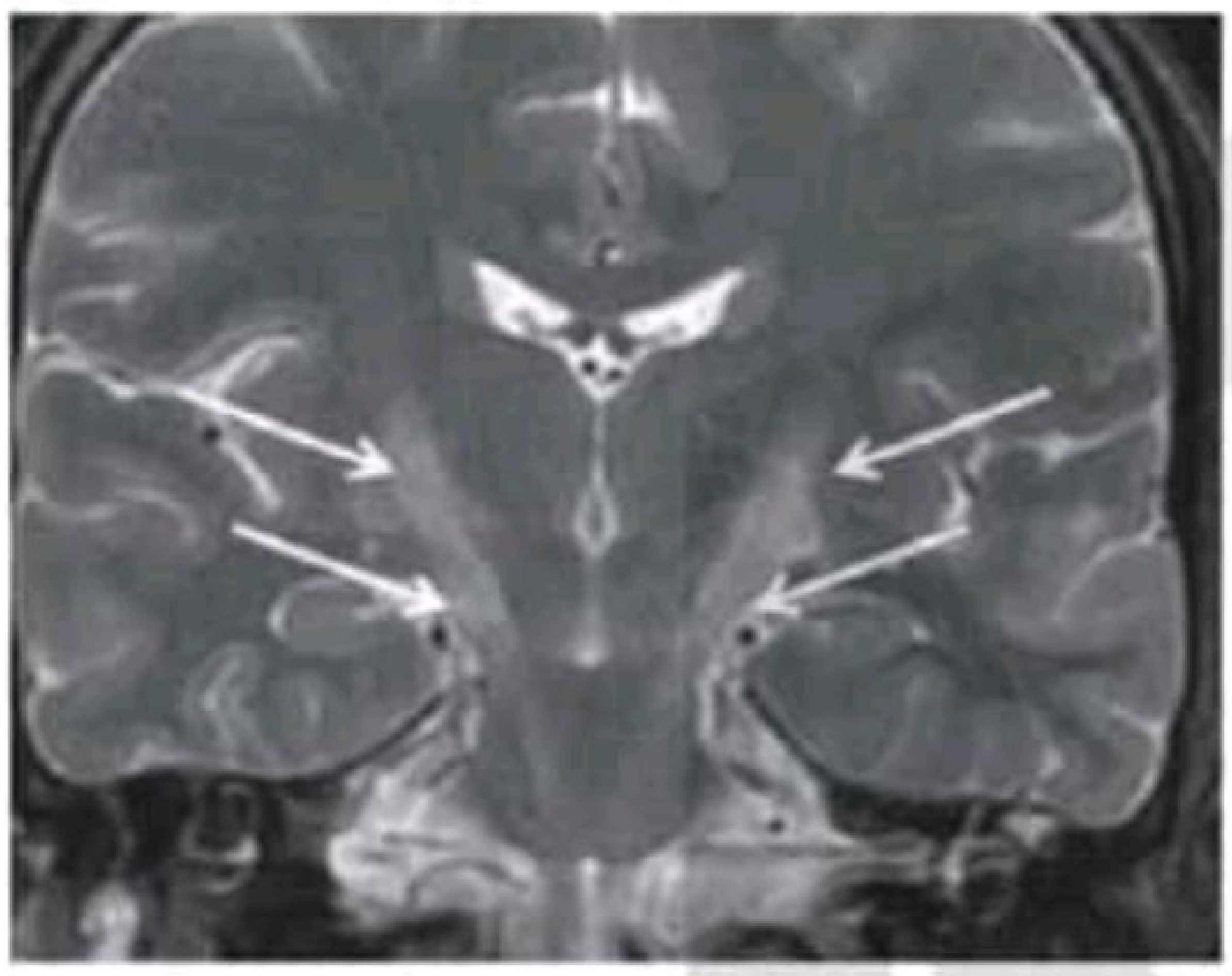


PUTAMINAL RIM SIGN
Seen in MSA-P

BOX CAR VENTRICLES
Thinning of caudate nucleus and dilatation of lateral ventricles.

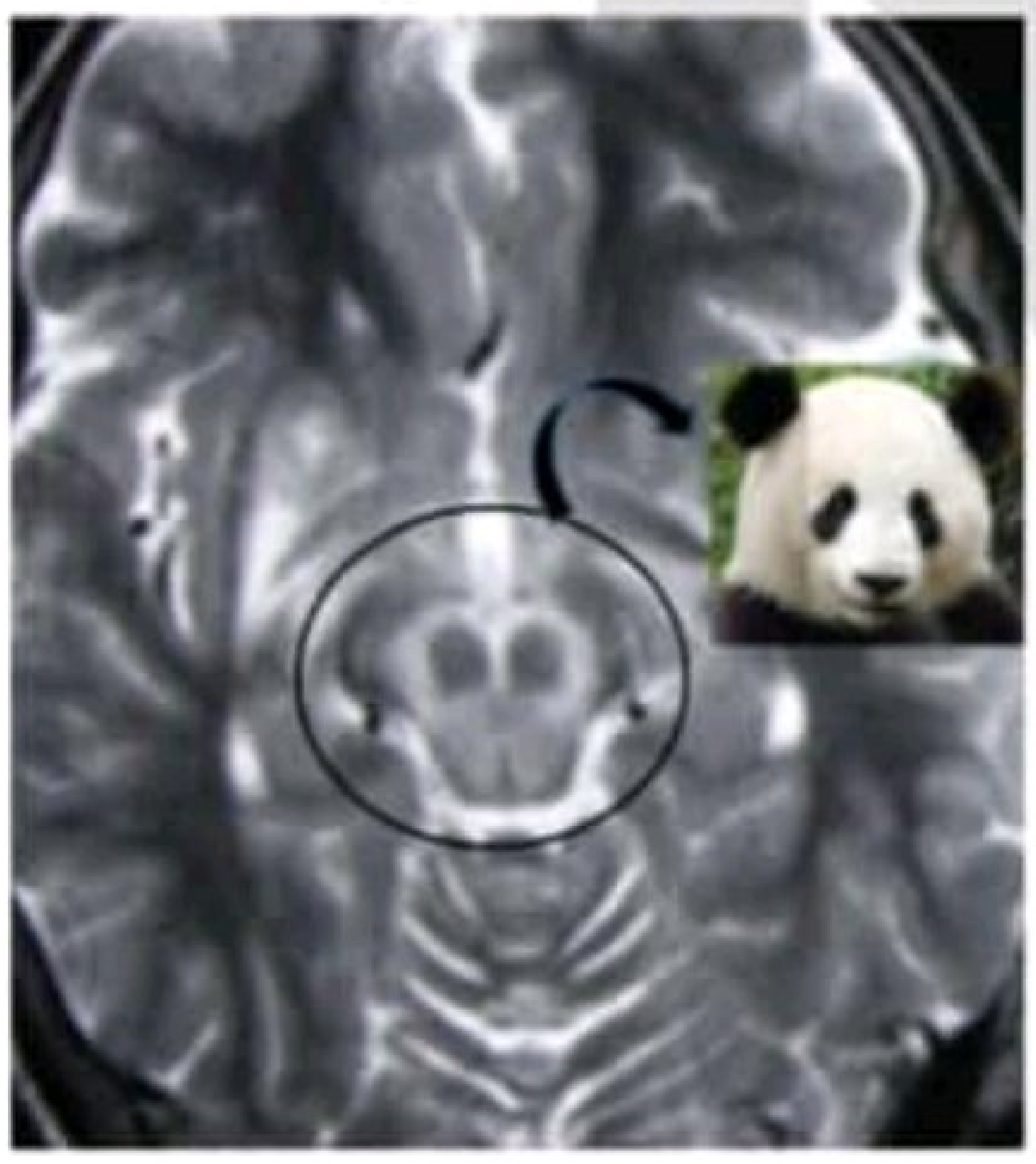
Dx: Huntington's Chorea.



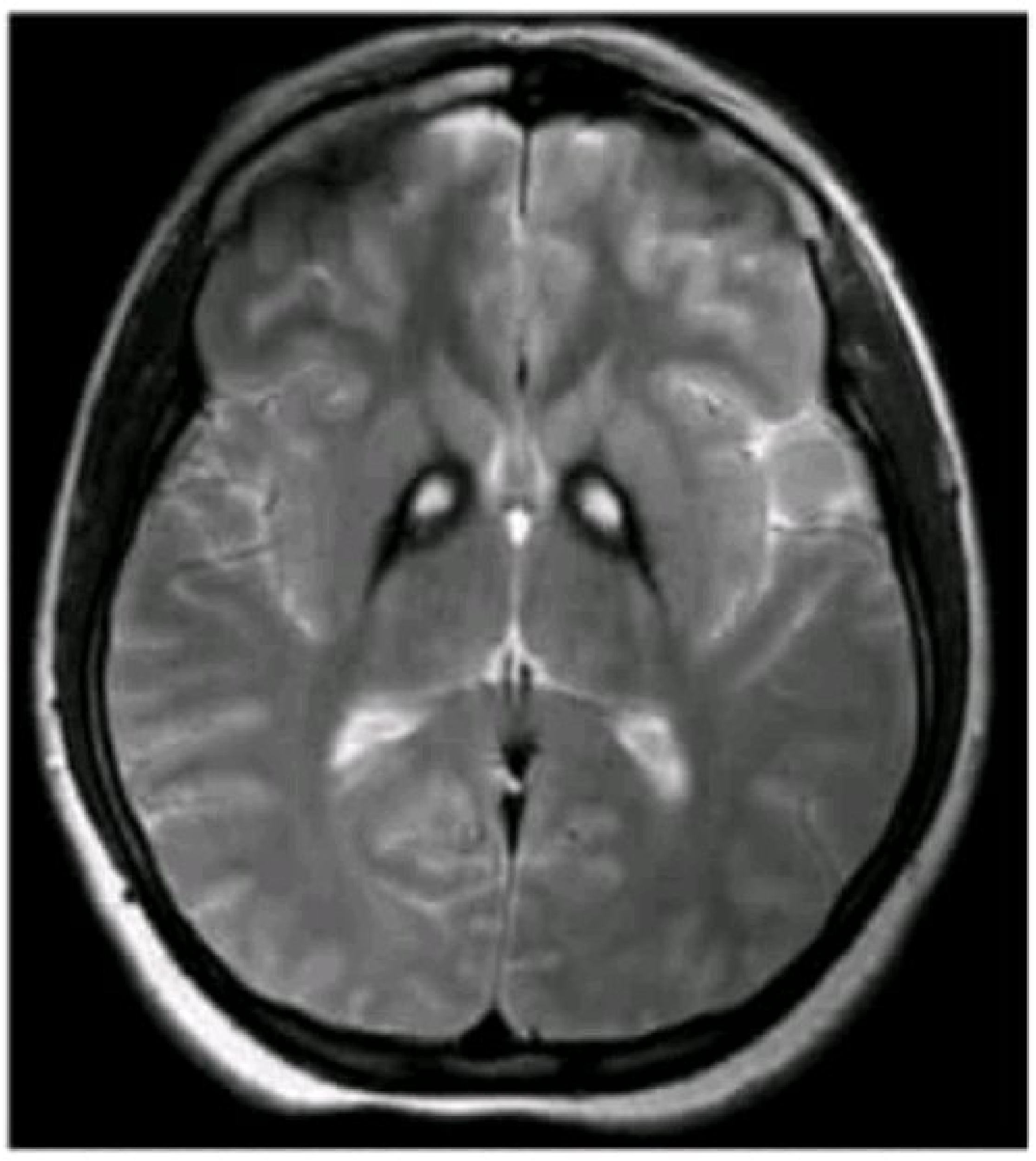


Hyperintense corticospinal tracts giving rise to **"WINE GLASS PATTERN"**

Seen in: Amyotrophic Lateral Sclerosis (ALS)



Face of giant panda sign
Due to abnormality of midbrain and sparing of Substantia Nigra & Red nucleus.



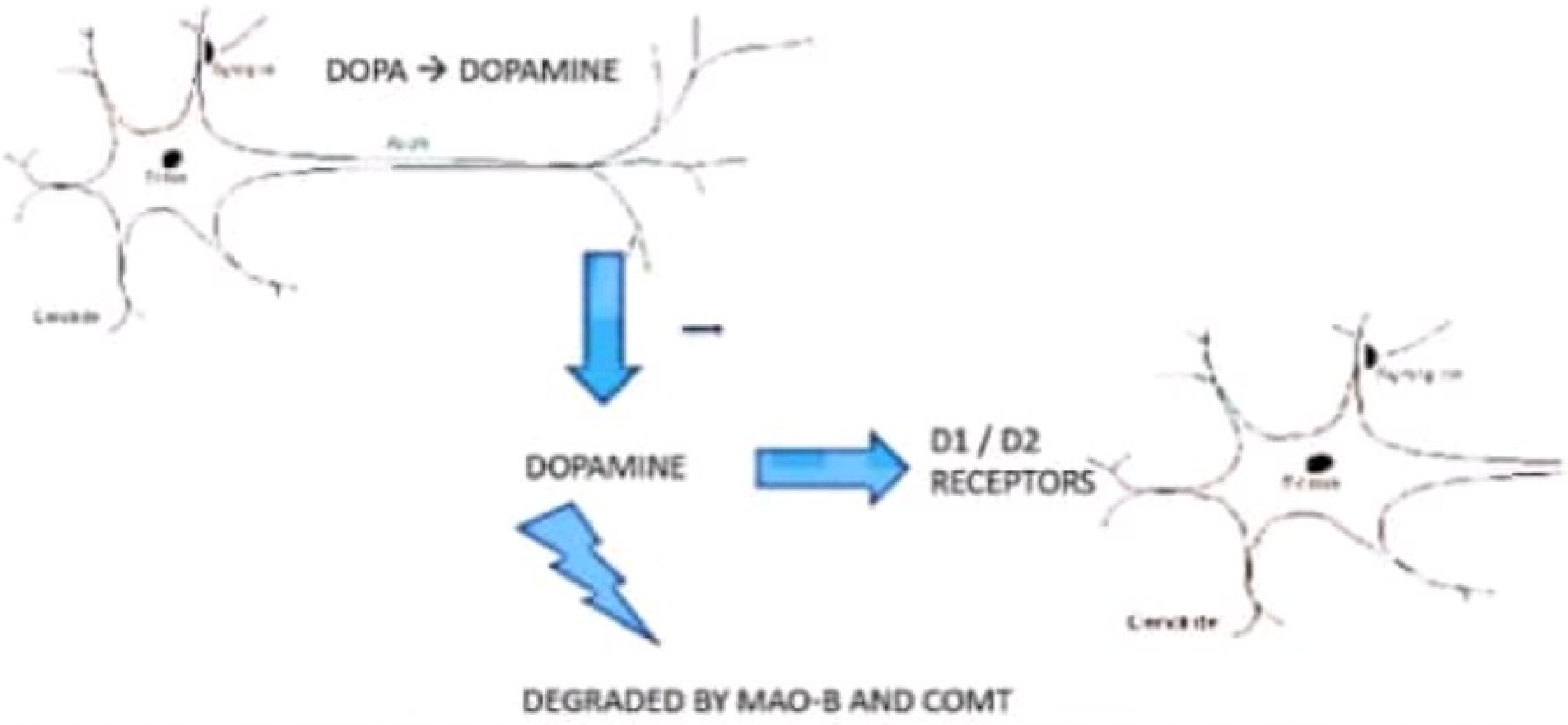
EYE OF TIGER SIGN
Seen in: NBIA

Neurodegeneration of Brain with Iron Accumulation (NBIA)

HALLEVORDEN SPATZ

Pentothenate Kinase Associated Neurodegeneration (PKAN)
Pathology: Iron deposits in Globus Pallidus

DRUG THERAPY FOR PARKINSONS DISEASE



LEVODOPA (L-DOPA)

PRODRUG: CONVERTED TO DOPAMINE BY DOPAMINE DECARBOXYLASE

SYNERGISM: CARBIDOPA, BENSARAZIDE
ANTAGONISM: PYRIDOXINE

CONTRAINDICATED: ANGLE CLOSURE GLAUCOMA, MELANOMA

PERIPHERAL DOPA DECARBOXYLASE INHIBITOR	CARBIDOPA, BENSARAZIDE
MAO-B INHIBITORS (IRREVERSIBLE)	SELIGILINE, RASAGILINE
MAO-B INHIBITORS (REVERSIBLE)	SAFINAMIDE
COMT INHIBITORS	ENTACAPONE, TOLCAPONE, OPICAPONE, NITECAPONE
NMDA ANTAGONIST	AMANTADINE
DOPAMINE AGONIST	ROPINROL, PRAMIPEXOLE (ORAL) ROTIGOTINE (TRNASDERMAL) APOMORPHINE (INJECTION)

MANAGEMENT OF PARKINSONISM

- NO FUNCTIONAL IMPAIRMENT: RASAGILINE (NEUROPROTECTIVE)
- FUNCTIONAL DISABILITY: LEVODOPA (OVERALL DOC) > ROPINROLE/PRAMIPEXOLE

INHIBIT PERIPHERAL DEGRADATION OF LEVODOPA:	CARBIDOPA, BENSARAZIDE
LEVODOPA INDUCED DYSKINESIA:	AMANTADINE
PROLONG ON PHASE:	ENTACAPONE > SELEGILINE/RASAGILINE/SAFINAMIDE > TOLCAPONE (DRUG OF LAST RESORT) ISTRADEFYLLINE (NEW DRUG)
RESCUE OFF PHASE:	APOMORPHINE
VOMITING:	DOMPERIDONE
PSYCHOSIS:	CLOZAPINE, QUETIPAINE, PIMAVANSERIN

LEVODOPA Is combined with BENZHEXOL (Anticholinergic) To control TREMORS due to Levodopa

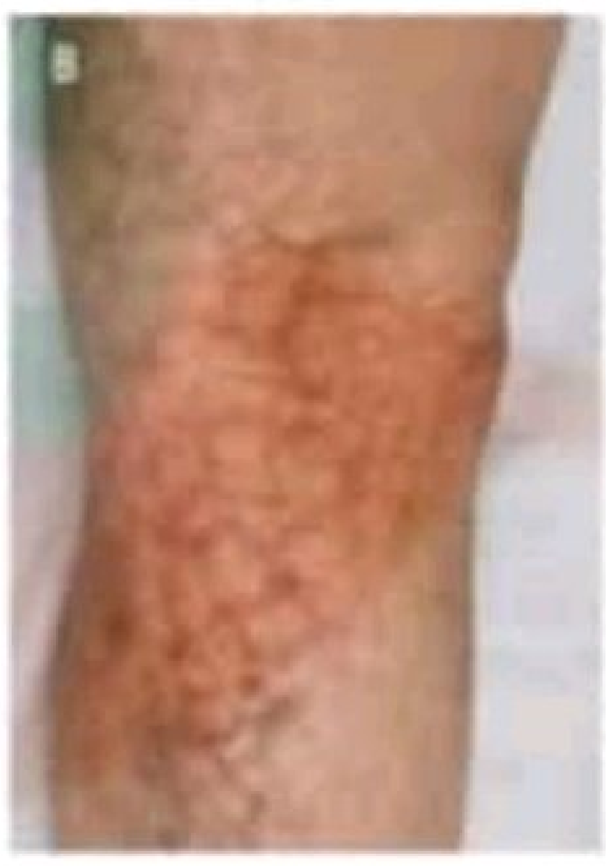
RESTLESS LEG SYNDROME

ROPINROL (DOC)
PRAMIPEXOL

AMANTADINE

USE: ANTI-INFLUENZAE VIRAL

S/E: LIVEDO RETICULARIS



HUNTINGTONS DISEASE

- VMAT-2 INHIBITORS (DOPAMINE DEPLETERS)
- TETRABENAZINE (DOC)
- DEUTETRABENZINE
- VALBENAZINE

TOURETTE SYNDROME

DOC: GUANFACINE > CLONIDINE

↓

ATYPICAL ANTIPSYCHOTICS: RISPERIDONE, OLANZAPINE, ZIPRASIDONE

↓

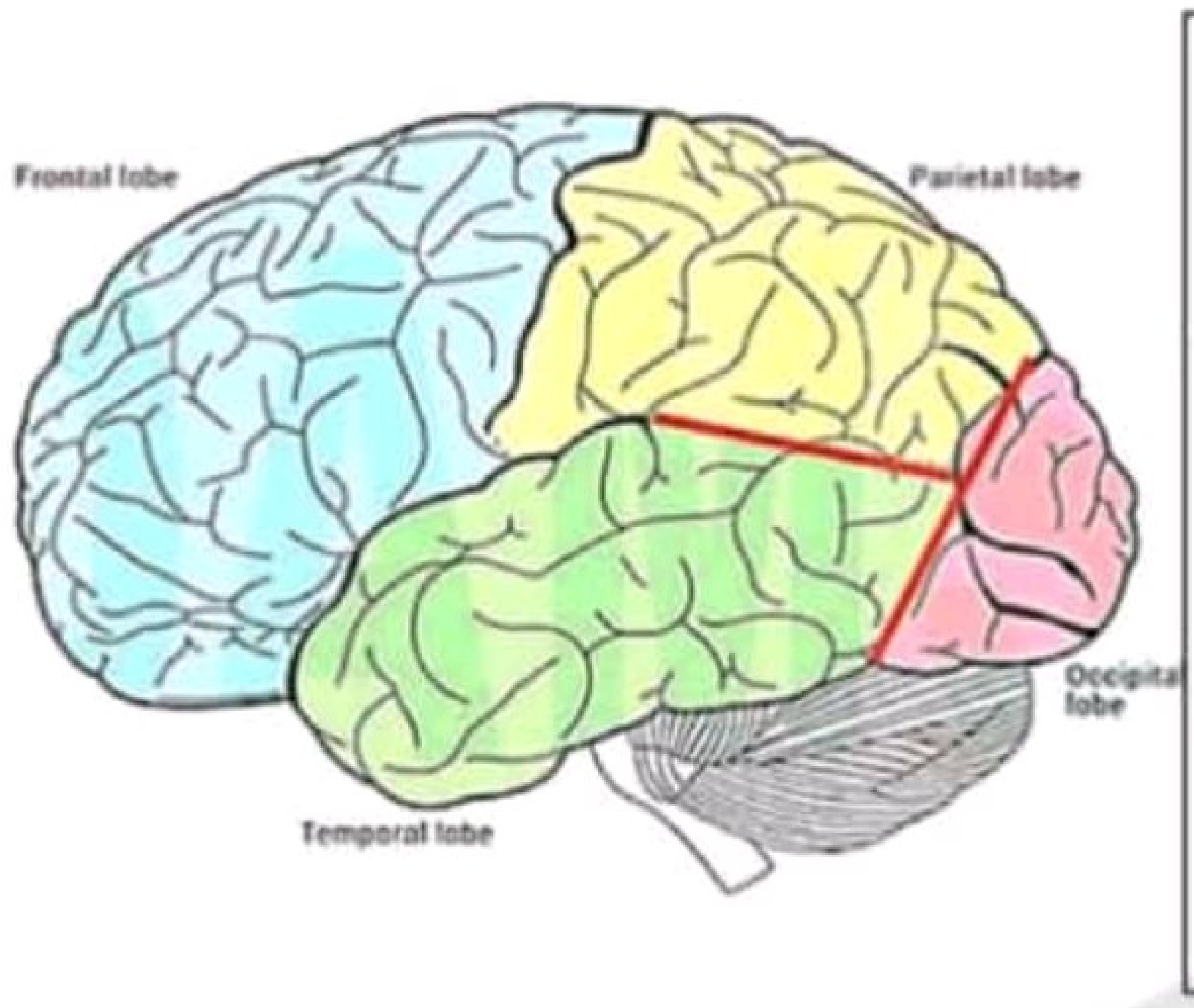
TYPICAL ANTIPSYCHOTICS: HALOPERIDOL, FLUPHENAZINE, PIMOZIDE

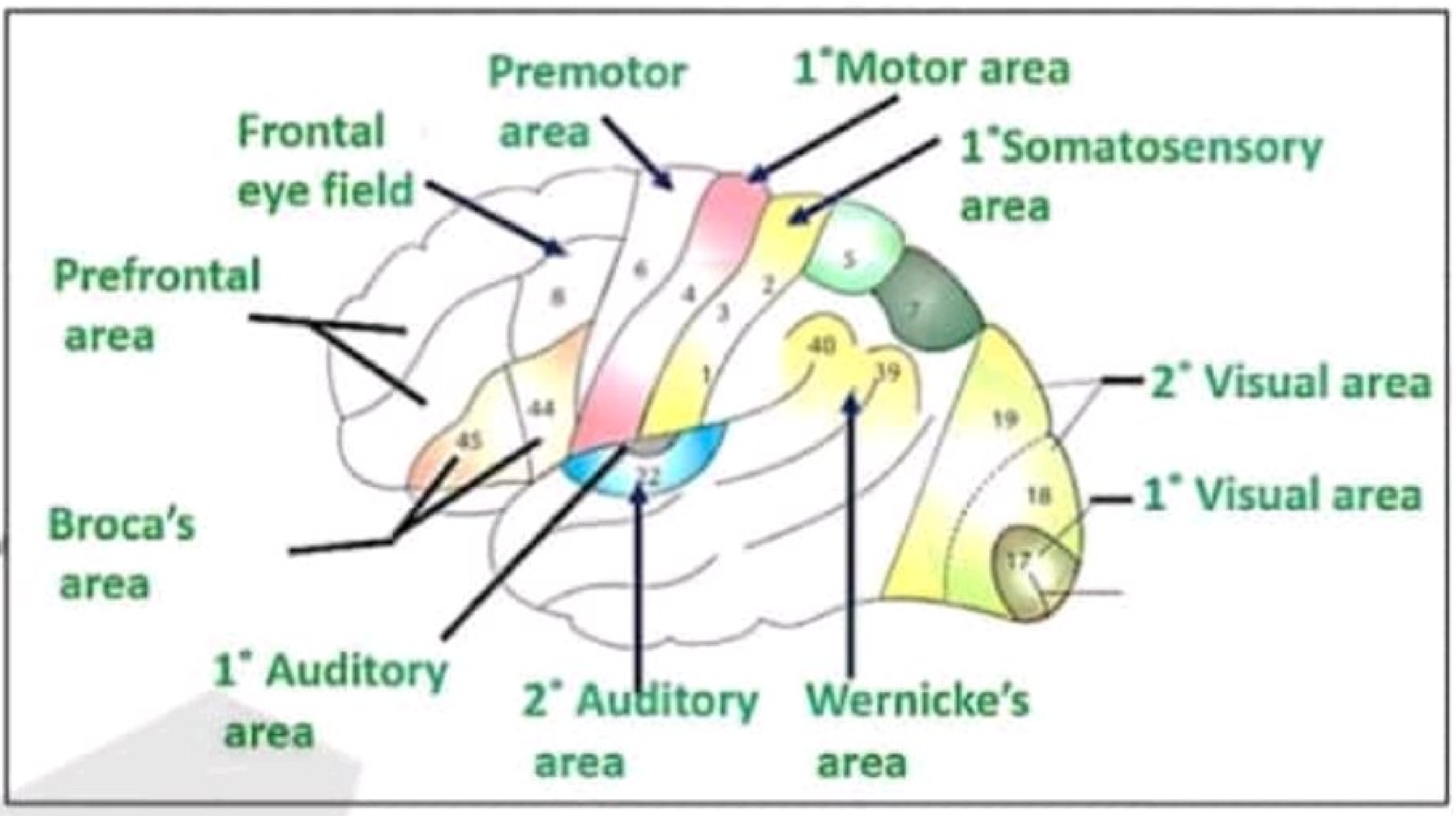
AMYOTROPHIC LATERAL SCLEROSIS

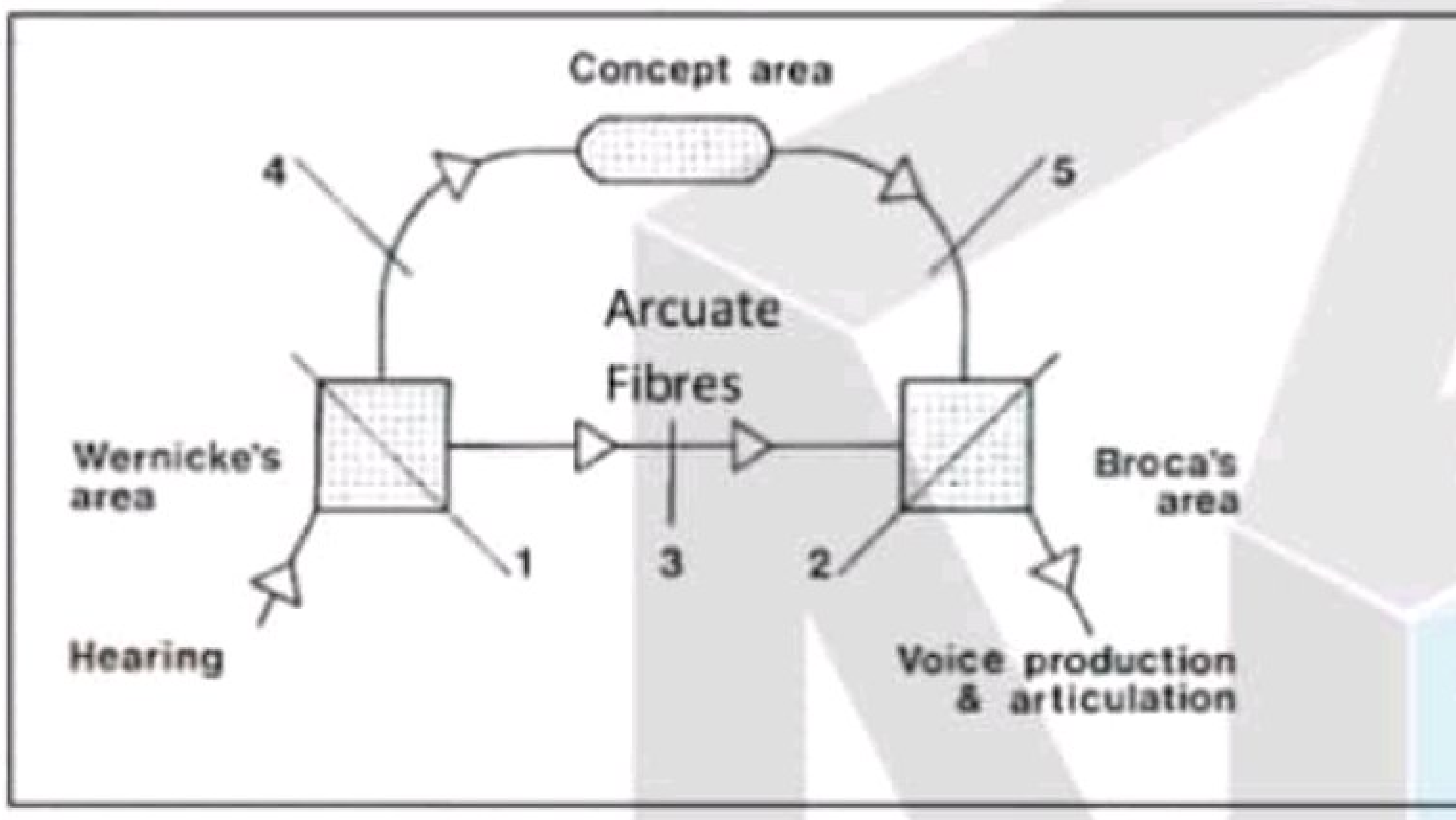
- RILUZOLE : NMDA ANTAGONIST
- EDARAVONE: ANTIOXIDANT

ALS is often called Lou Gehrig's disease

CEREBROVASCULAR ACCIDENTS


Frontal lobe
Parietal lobe
Occipital lobe
Temporal lobe


Premotor area
1° Motor area
Frontal eye field
1° Somatosensory area
Prefrontal area
2° Visual area
1° Visual area
Broca's area
1° Auditory area
2° Auditory area
Wernicke's area
45
44
8
6
4
3
2
1
5
7
40
39
22
19
18
17


Concept area
4
5
Arcuate Fibres
Wernicke's area
Broca's area
1
3
2
Hearing
Voice production & articulation

APHASIA

1-WERNICKE

2-BROCA

3-CONDUCTION

4-TC SENSORY

5-TC MOTOR

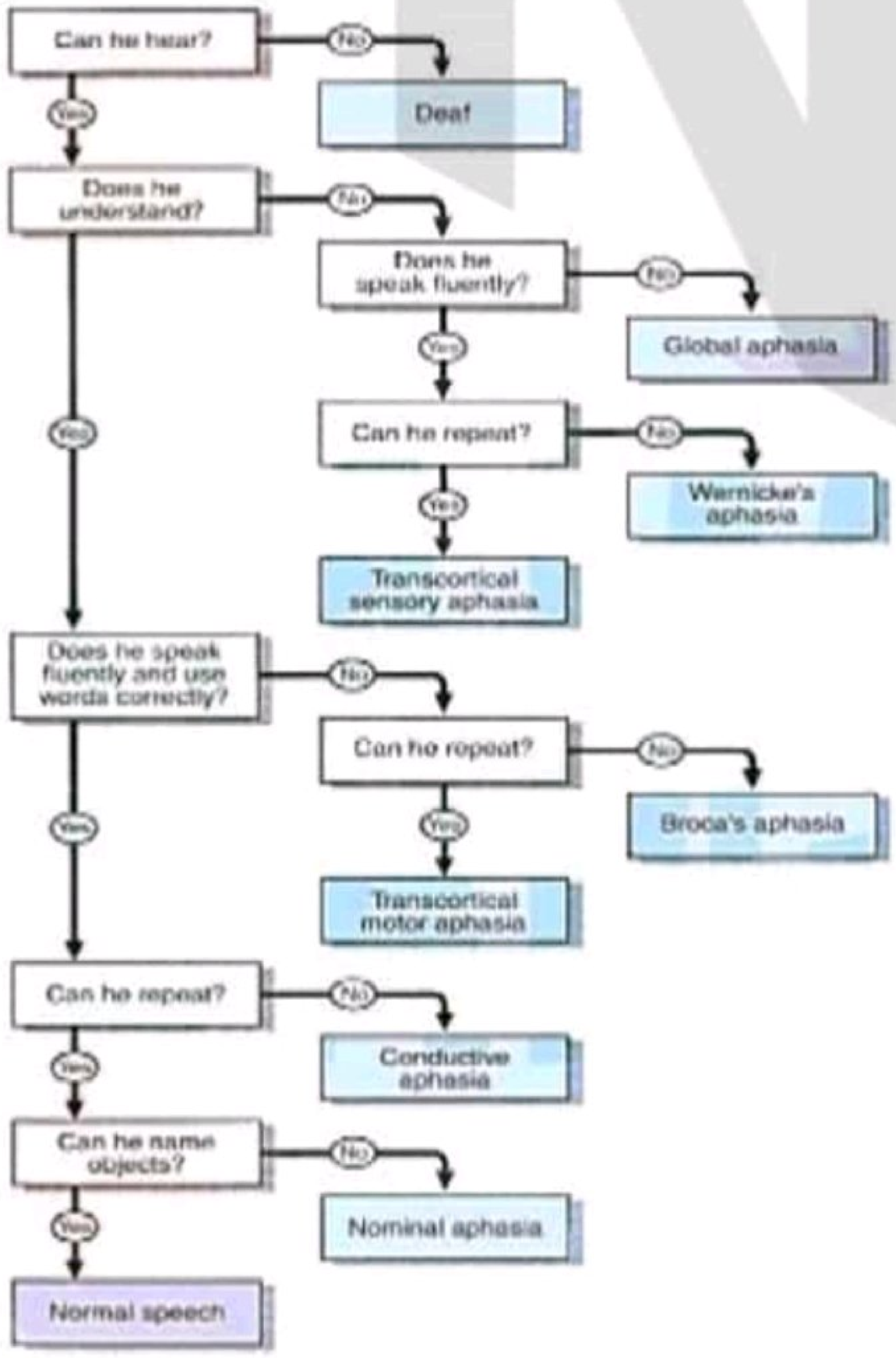
Broca's = 44+45

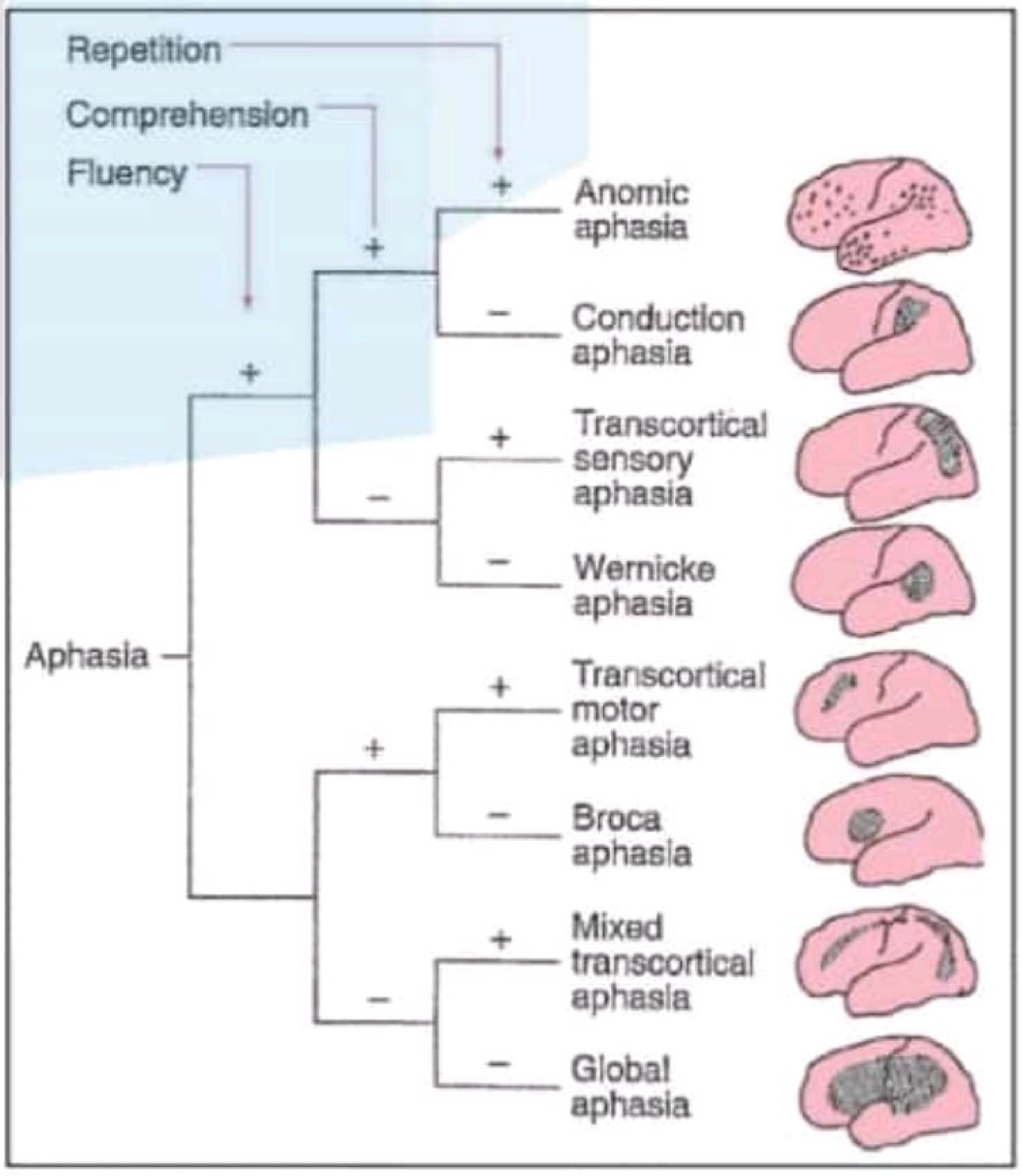
Wernicke's= 39 +40 +22 areas

Concept Area: Naming

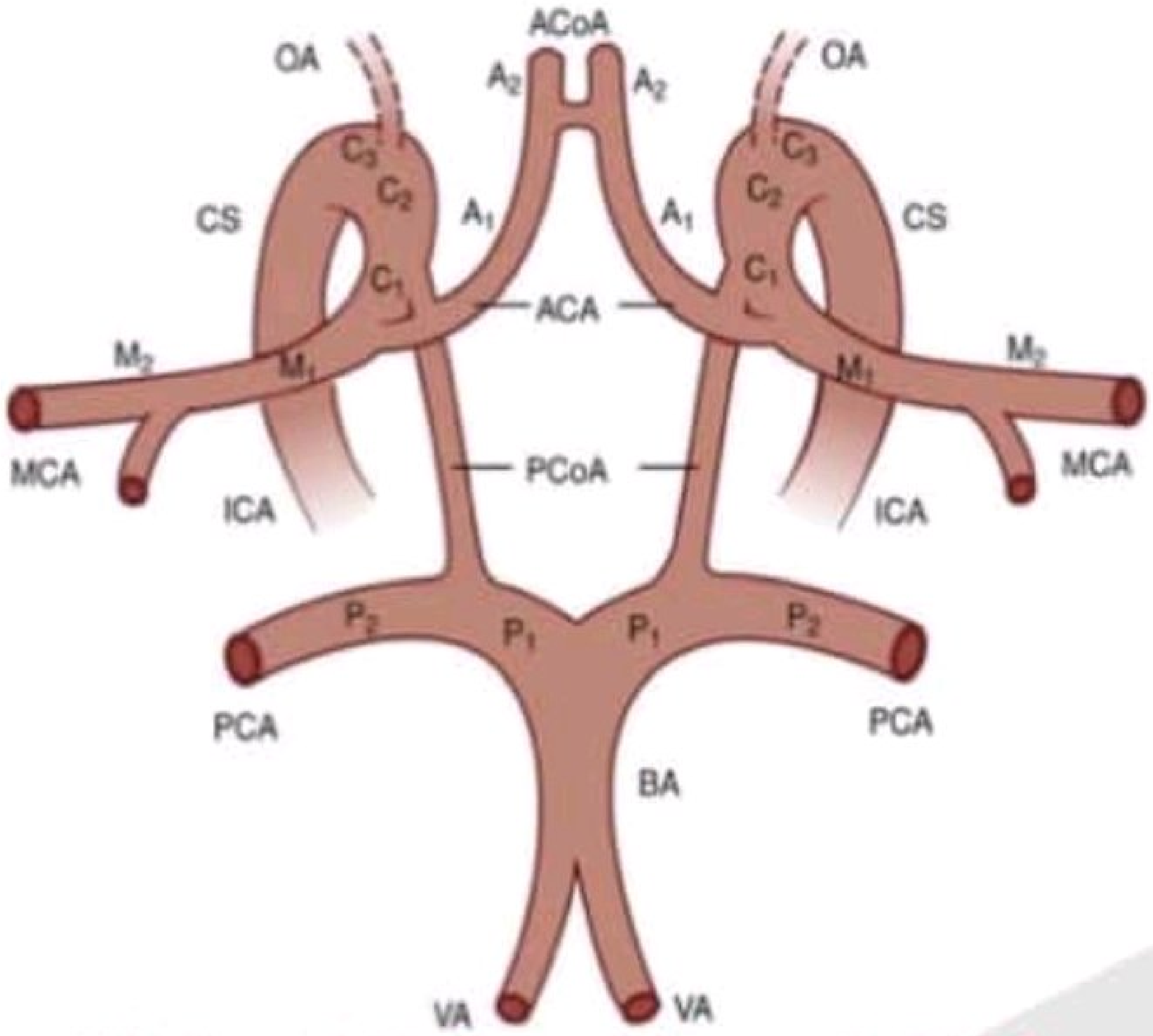
Arcuate Fibres: Repetition

TC: Transcortical

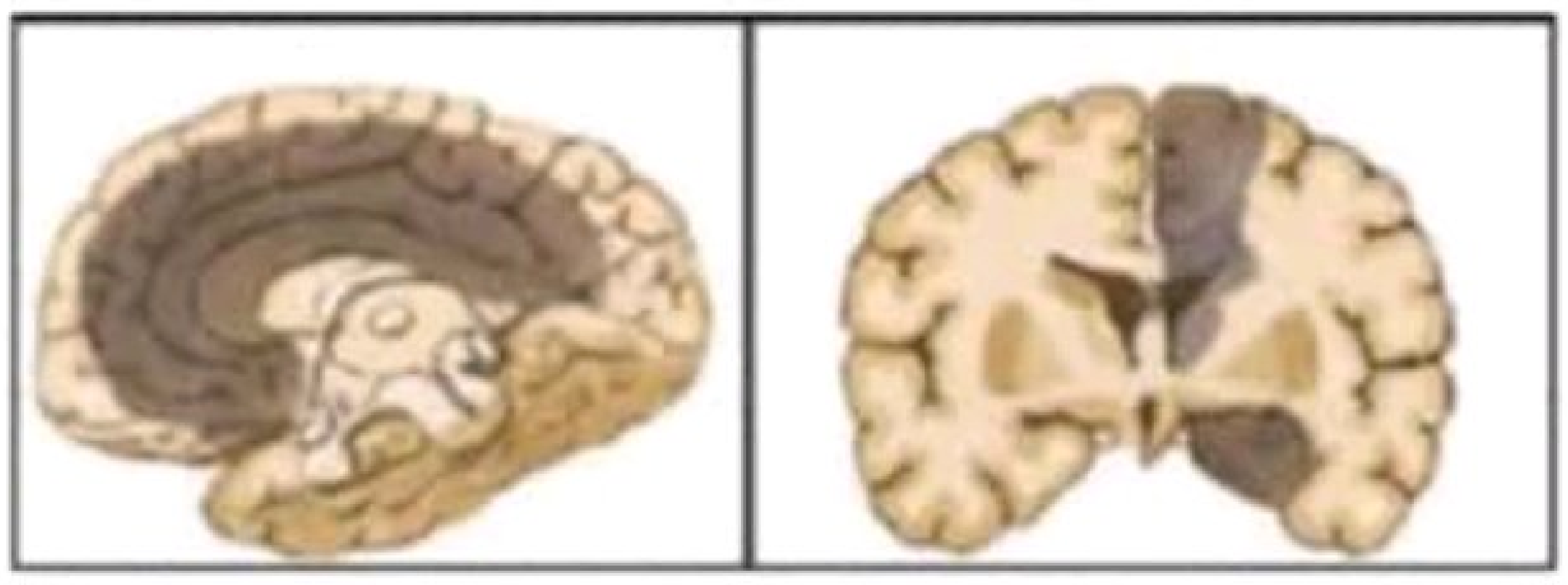

Can he hear?
No
Deaf
Yes
Does he understand?
No
Does he speak fluently?
No
Global aphasia
Yes
Can he repeat?
No
Wernicke's aphasia
Yes
Transcortical sensory aphasia
Yes
Does he speak fluently and use words correctly?
No
Can he repeat?
No
Broca's aphasia
Yes
Transcortical motor aphasia
Yes
Can he repeat?
No
Conductive aphasia
Yes
Can he name objects?
No
Nominal aphasia
Yes
Normal speech


Repetition
Comprehension
Fluency
Aphasia
+
+
+
Anomic aphasia
−
Conduction aphasia
−
+
Transcortical sensory aphasia
−
Wernicke aphasia
−
+
+
Transcortical motor aphasia
−
Broca aphasia
−
+
Mixed transcortical aphasia
−
Global aphasia

ACA INFARCTS


ACoA
OA
OA
A2
A2
C3
C3
C2
C2
CS
CS
A1
A1
C1
C1
ACA
M2
M2
M1
M1
MCA
MCA
ICA
ICA
PCoA
P2
P2
P1
P1
PCA
PCA
BA
VA
VA

ACA TERRITORY:

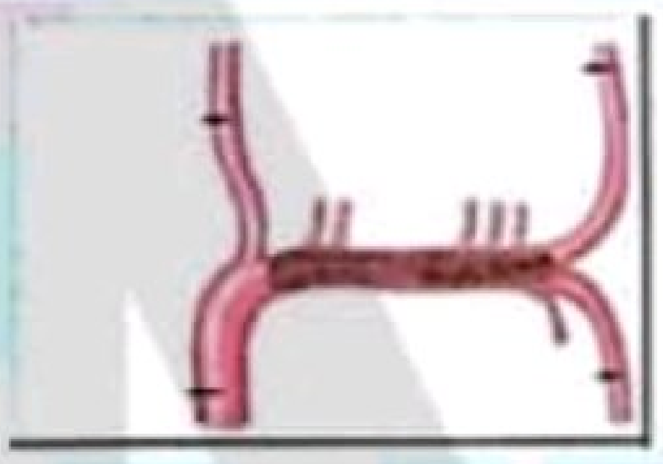
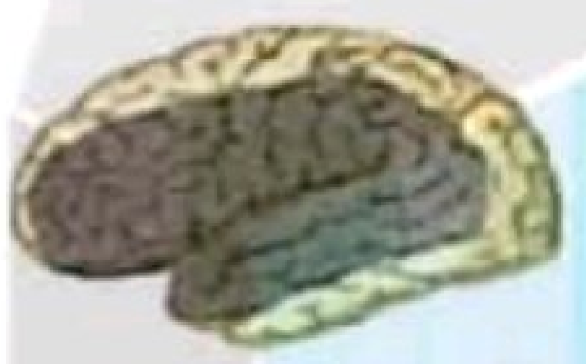
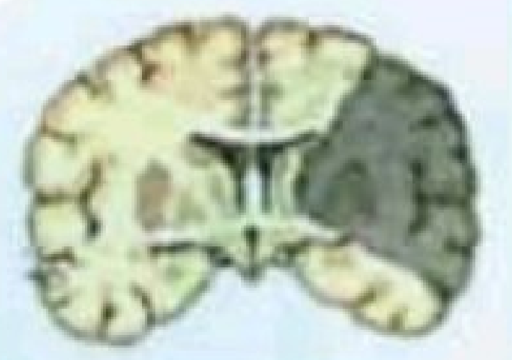
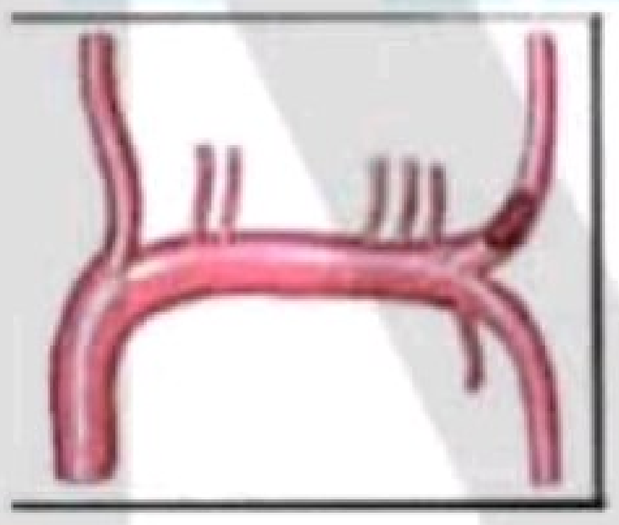
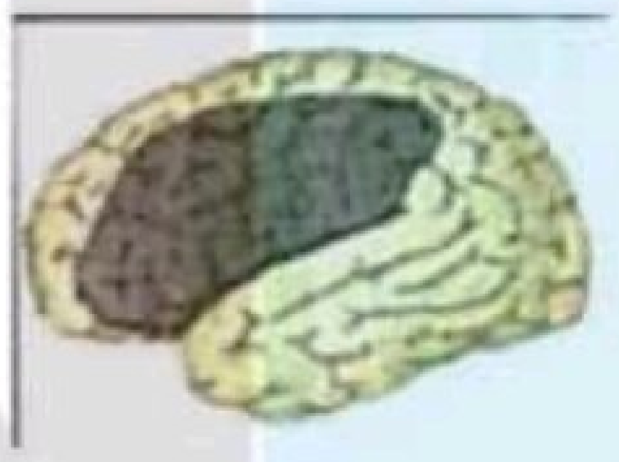
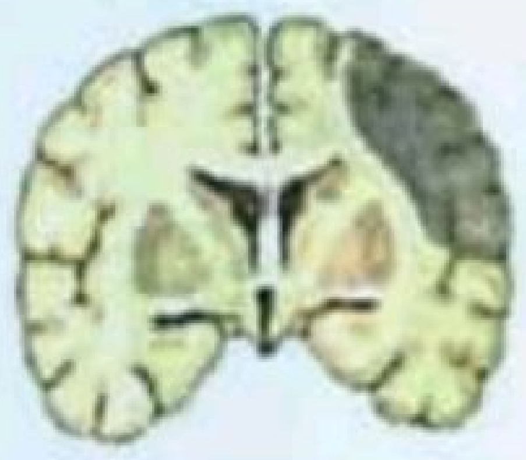
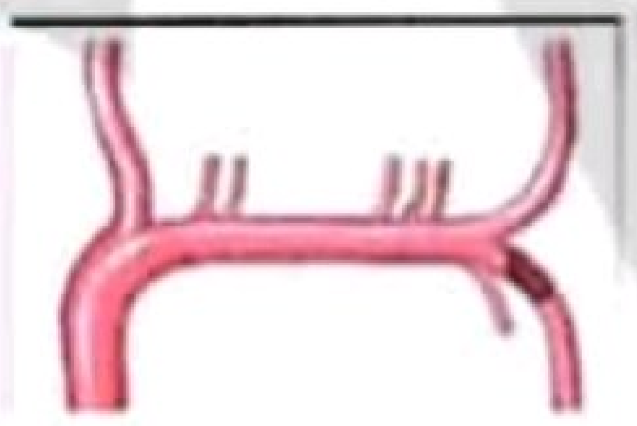
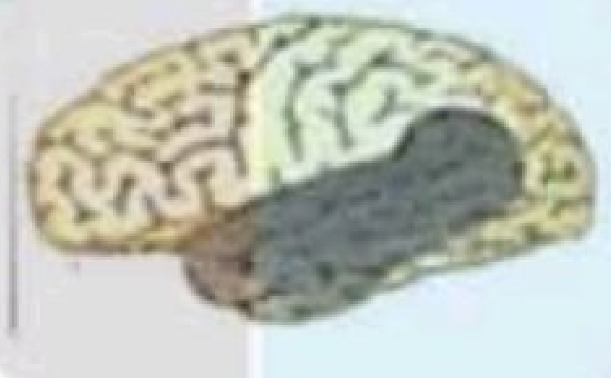
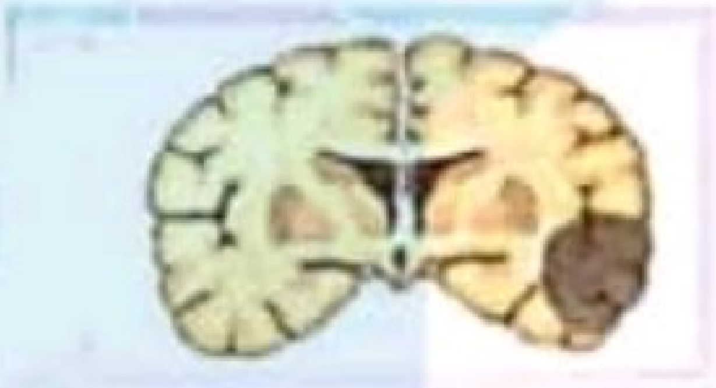


Clinical Features (If A2 Infarct)

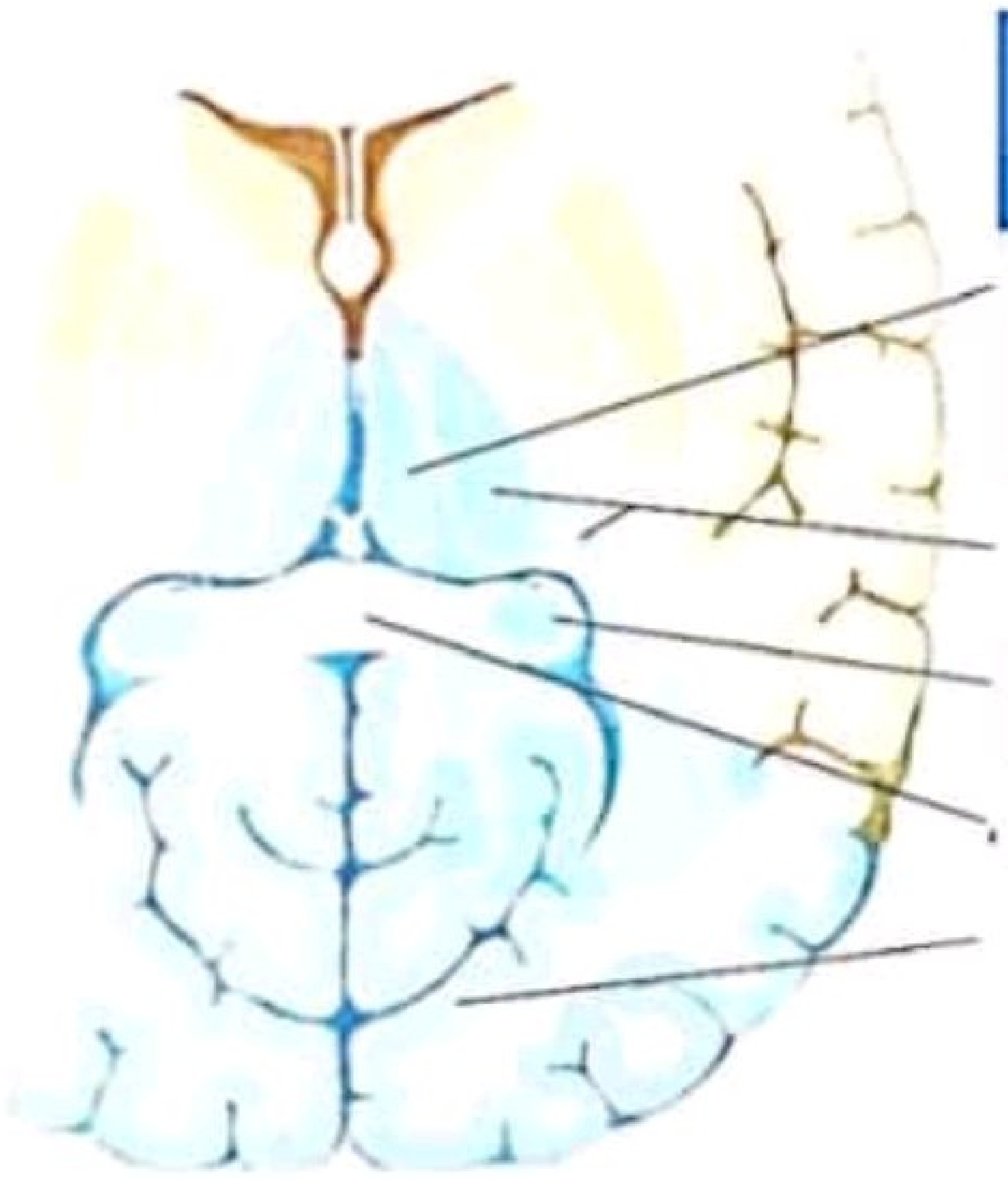
- C/L LL weakness → Paracentral Lobule
- Urinary incontinence → Paracentral Lobule
- Anti-social behaviour→Pre-Frontal area

If it is an A1 infarct, it's usually TIA because of compensatory reperfusion from ACoA

MCA INFARCTS

DIVISION		LATERAL VIEW	CORONAL VEIW	CLINICAL FEATURES
ENTIRE TERRITORY				C/L Hemiparesis Global aphasia
SUPERIOR				C/L Hemiparesis Broca's aphasia
INFERIOR				C/L Hemiparesis LT-Wernicke's aphasia RT-Constr dyspraxia

PCA INFARCT



AREA	DEFICIT
Medial Thalamus & Midbrain	Hypersomnolence,3rd nerve palsy ,behavioural alterations
Lateral Thalamus	Hemisensory loss
Hippocampus	Memory loss
Splenium of corpus callosum	Alexia without agraphia
Calcarine area	Hemianopsia

TREATMENT OF ISCHEMIC STROKE

- Thrombolysis
  - ✓ rtpa @0.9 mg/kg over 1 hour
  - ✓ Window period -4.5 hours
- Antiplatelets
  - ✓ Aspirin
- Anticoagulants

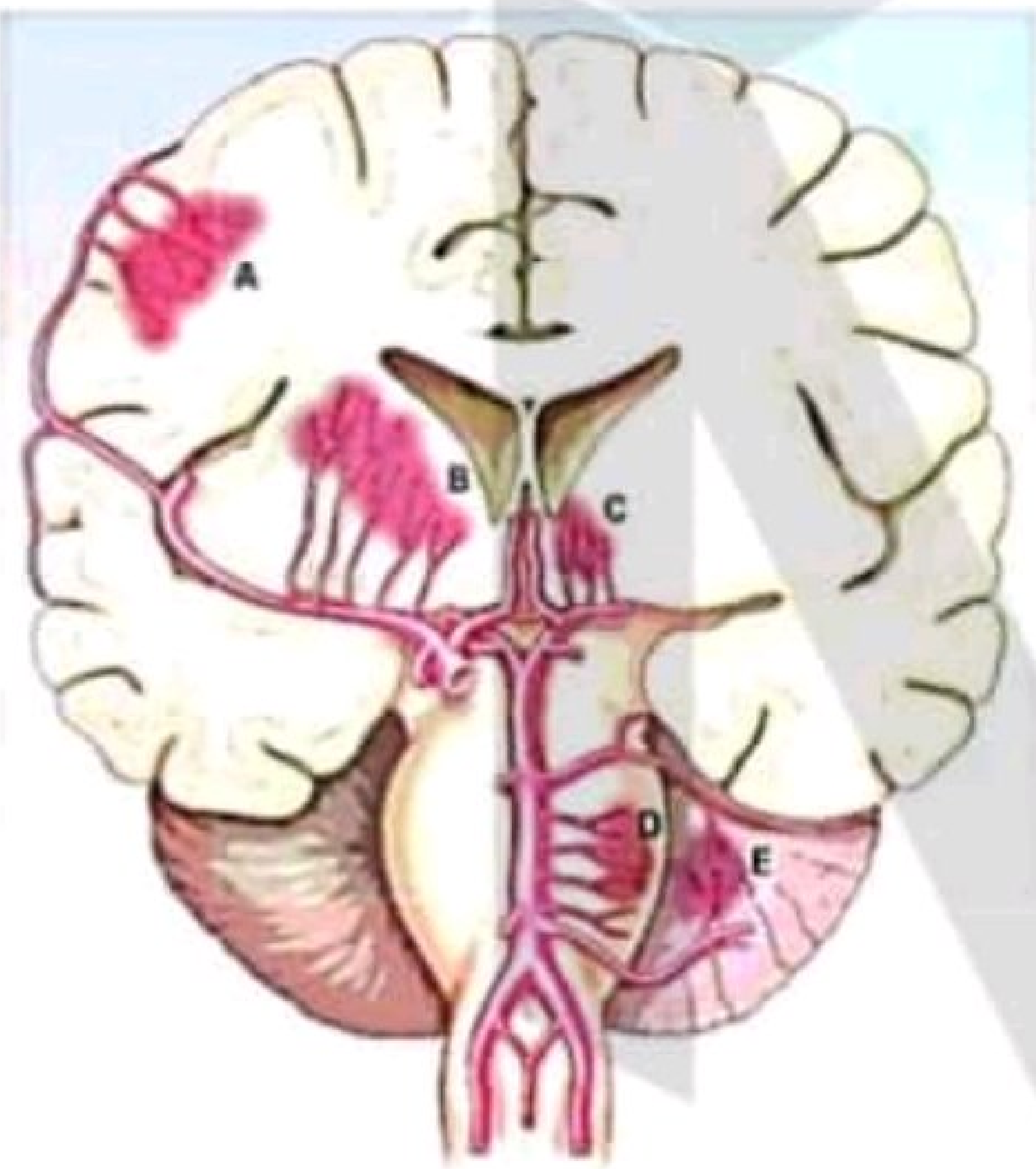
CHA2DS2 -VASc score

CRITERIA	SCORE
CHF	1
HTN	1
Age >75 yrs	2
DM	1
Prior Stroke /TIA	2
Vascular disease	1
Age 65 -74 yrs	1
Female Sex	1

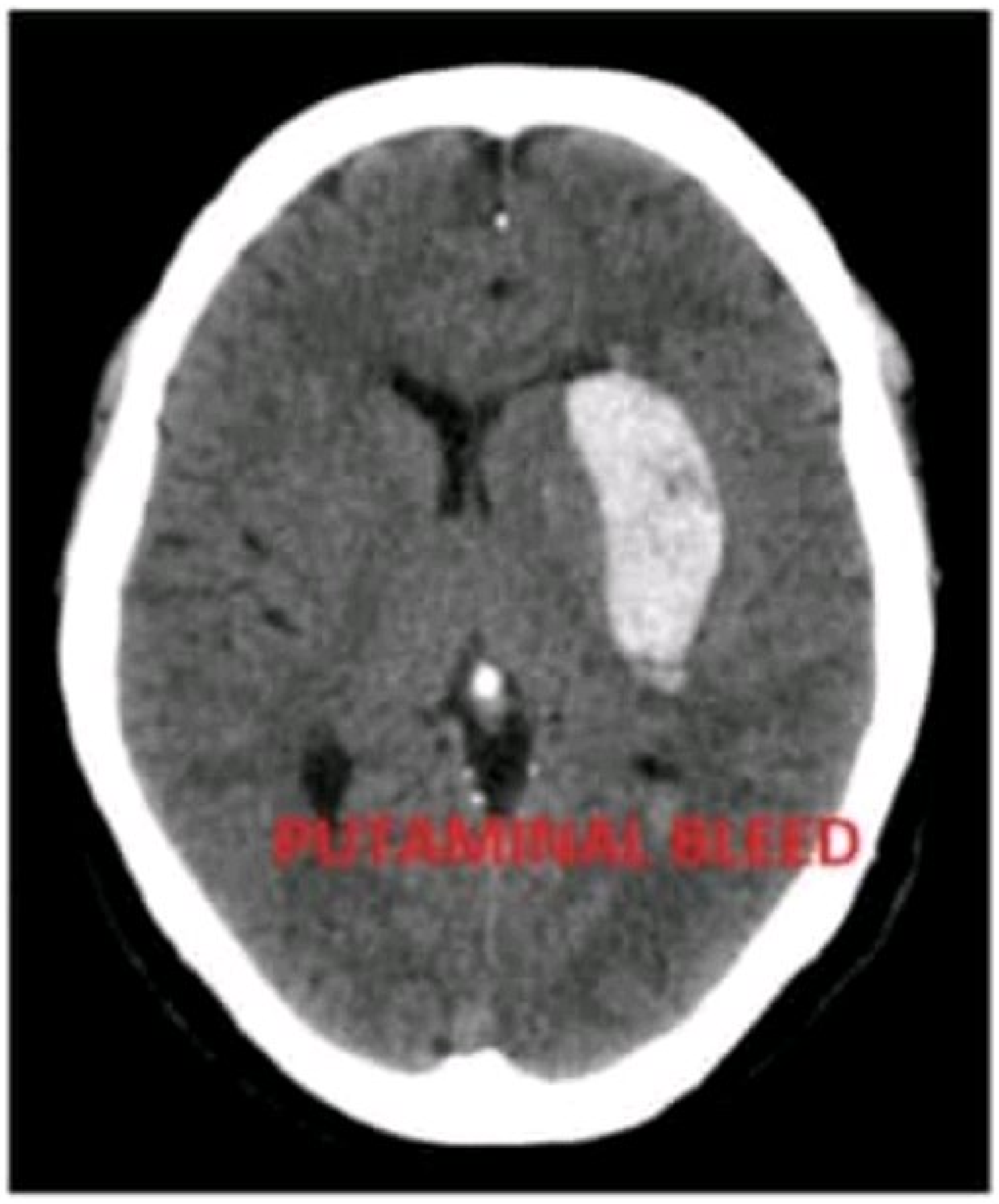
NON VALVULAR AF

SCORE	TREATMENT
0	ASPIRIN
1	ASP/OAC
2	OAC

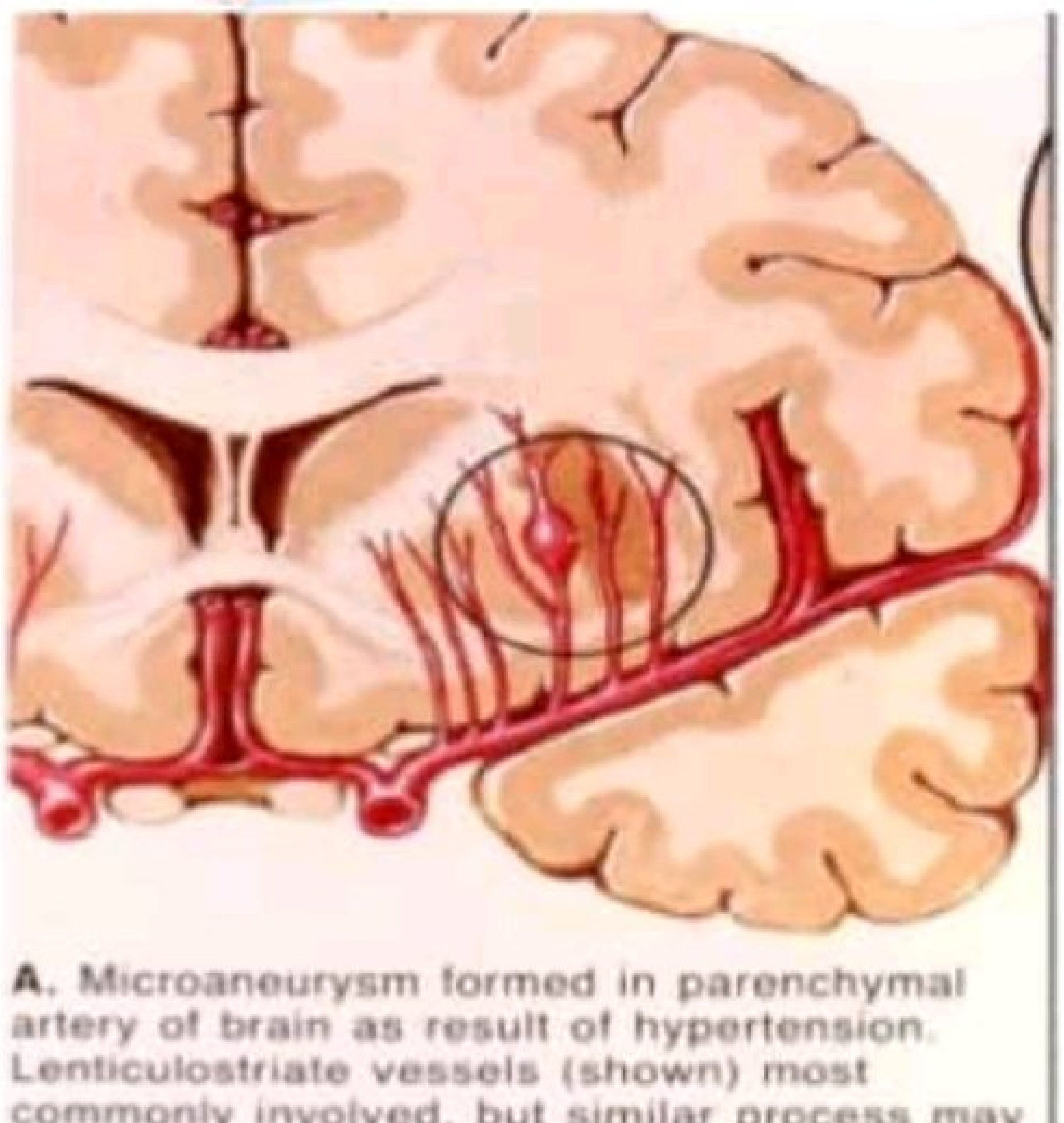
INTRACERERAL HEMMORHAGE



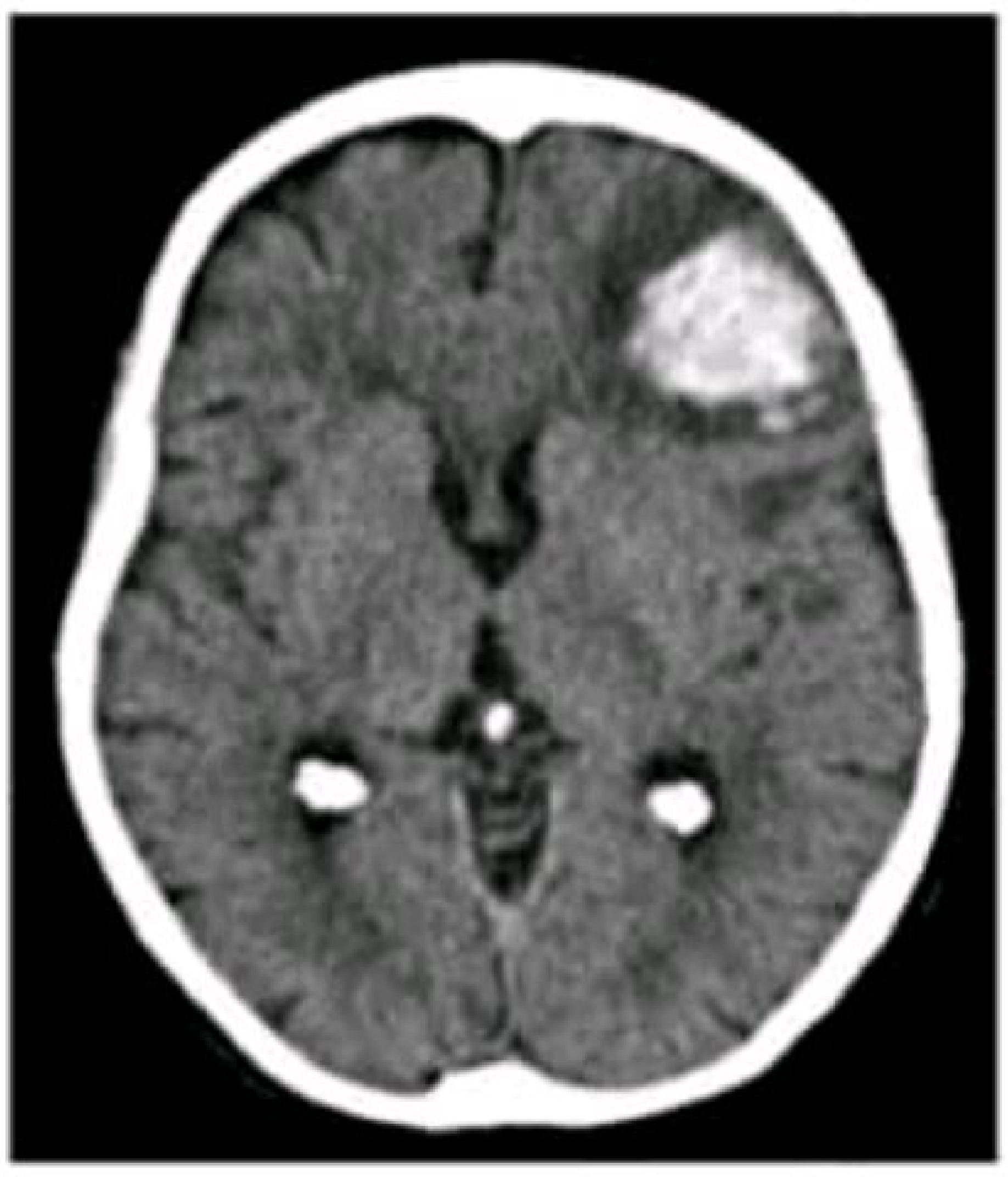
	AREA	DEFICIT
A	Cortex	Headache +Seizure +Lobar dysfunction
B	Putamen	Hemiparesis
C	Thalamus	Hemianesthesia
D	Pons	Quadriparesis with decerebrate rigidity
E	Cerebellum	Ataxia



Because of Charcot-Bouchard Aneurysm
M/C/C is Hypertension



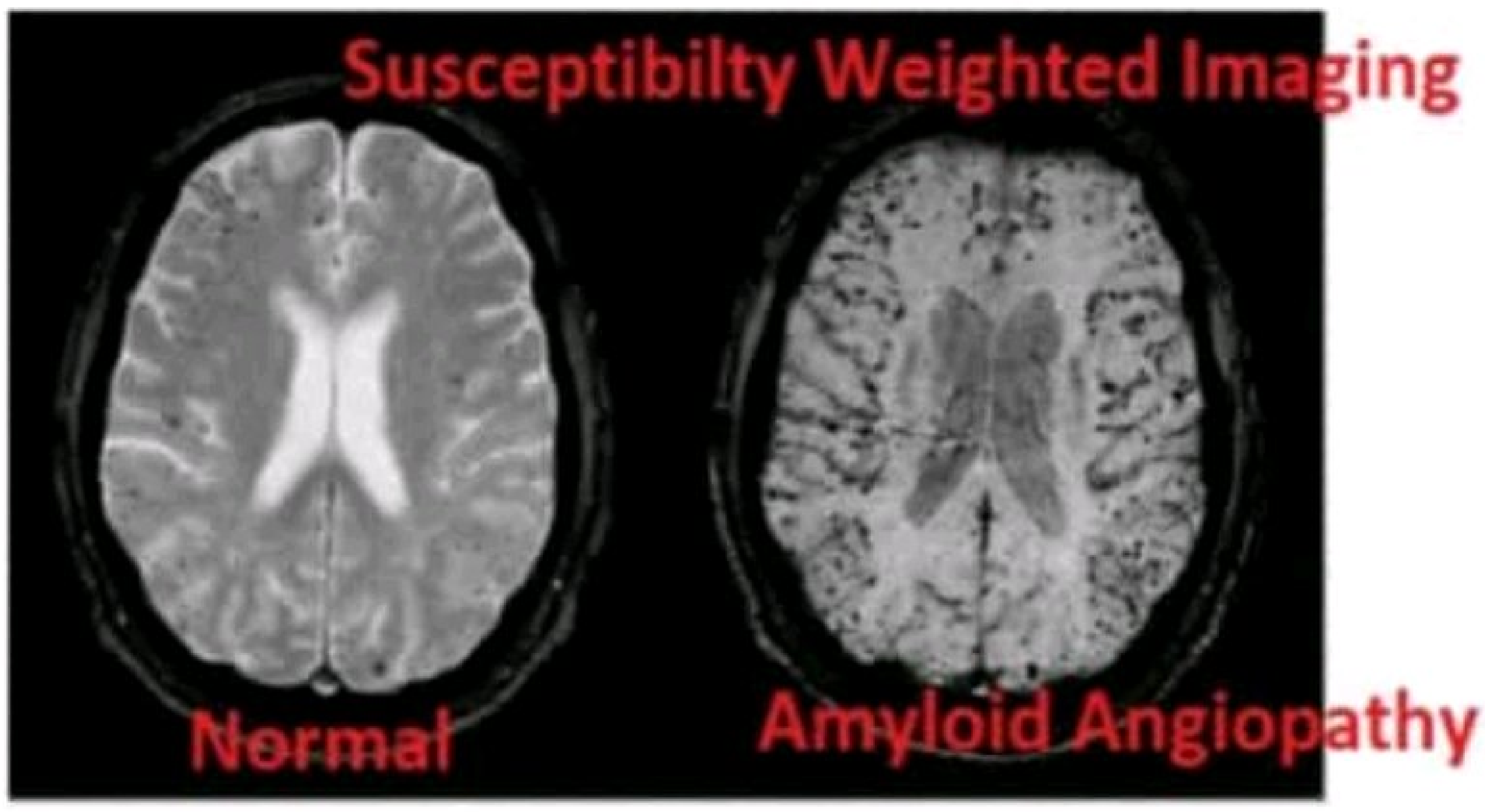
A. Microaneurysm formed in parenchymal artery of brain as result of hypertension. Lenticulostriate vessels (shown) most commonly involved, but similar process may occur in other parts of brain, especially lobar white matter, thalamus, pons and cerebellum



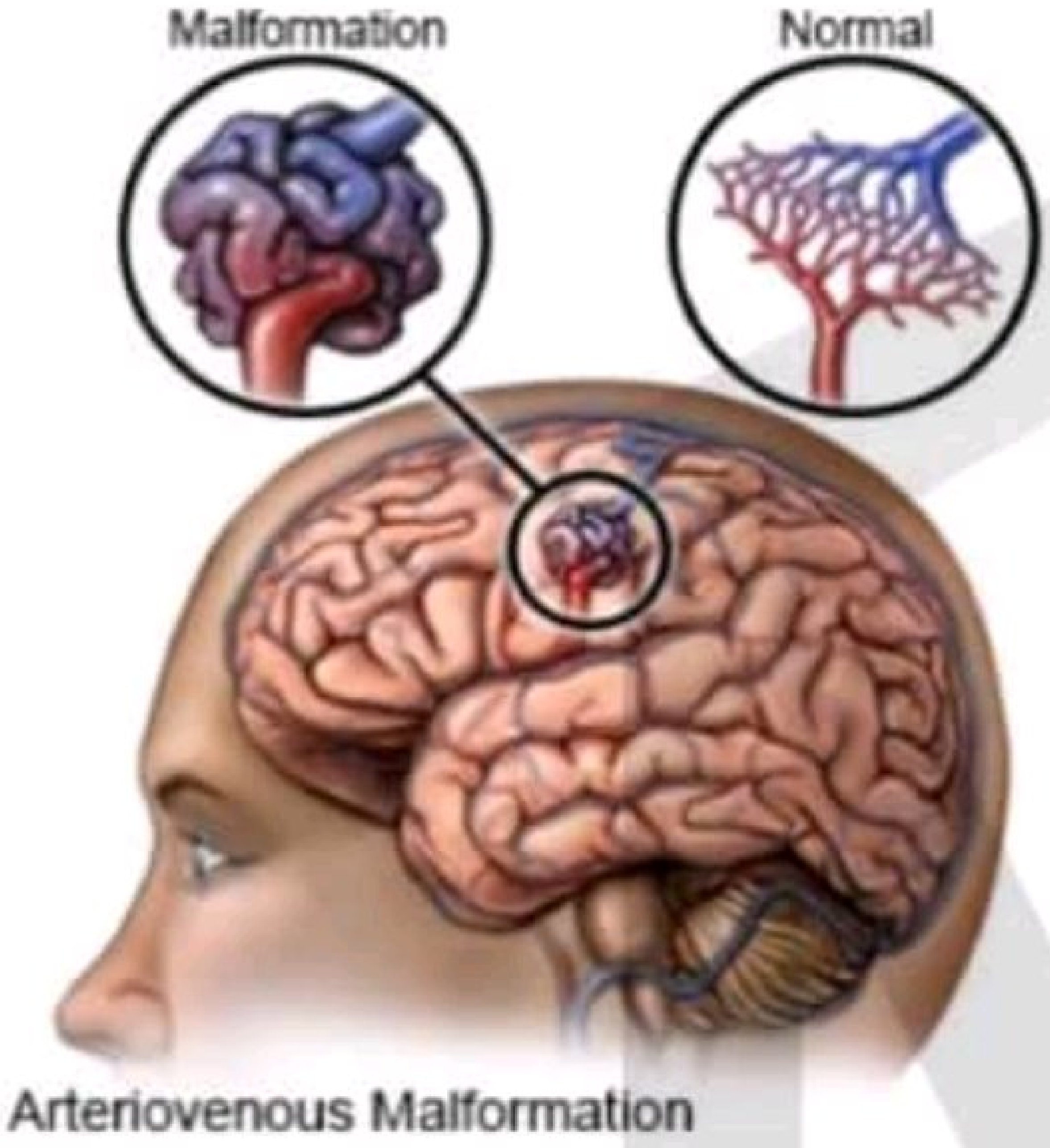
Infarct in Old Man

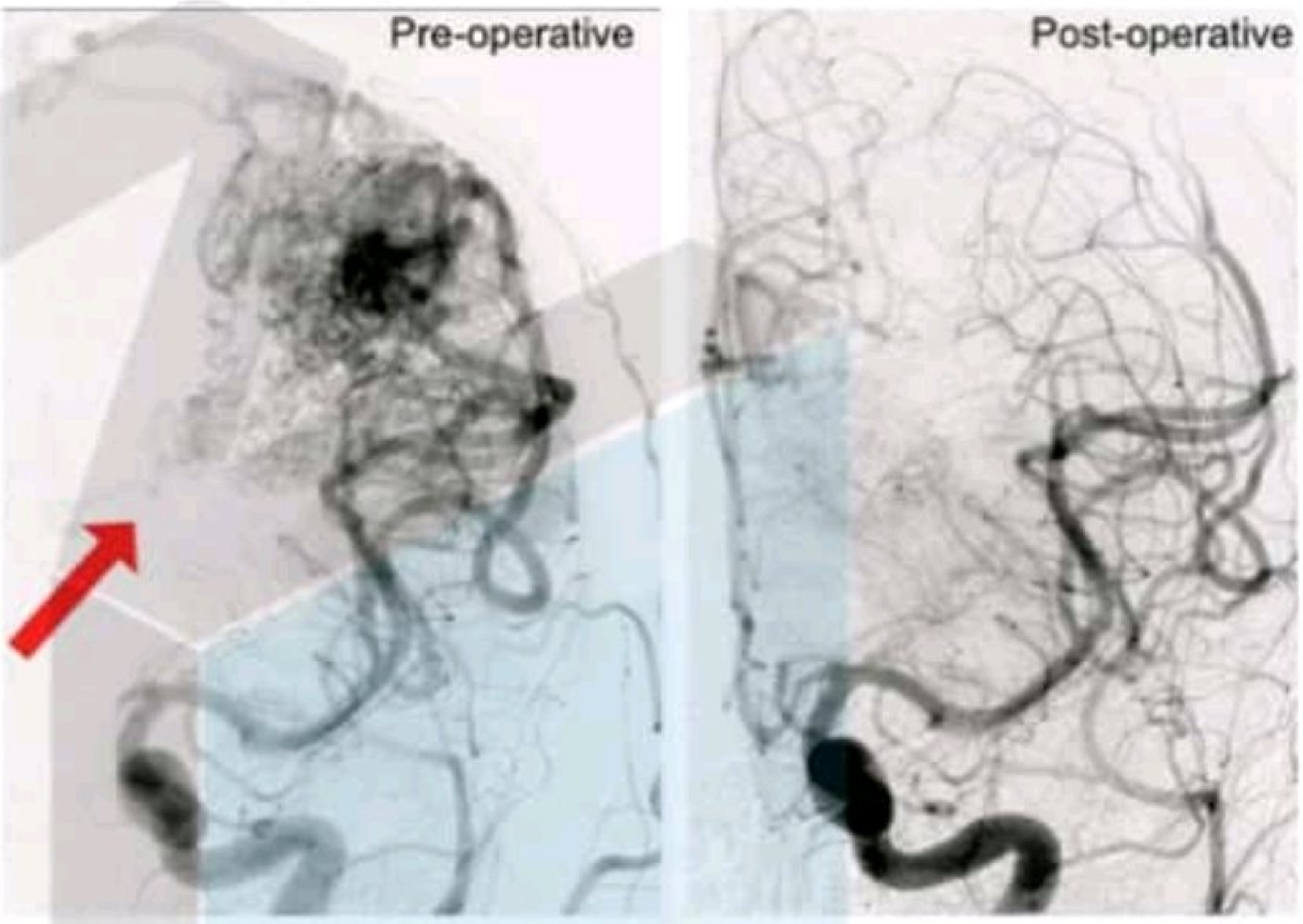
Lobar Hematoma

M/C/C:
Amyloid Angiopathy


Susceptibilty Weighted Imaging
Normal
Amyloid Angiopathy

Another cause of INFARCT in YOUNG patients is AVM- Arterio-venous Malformation

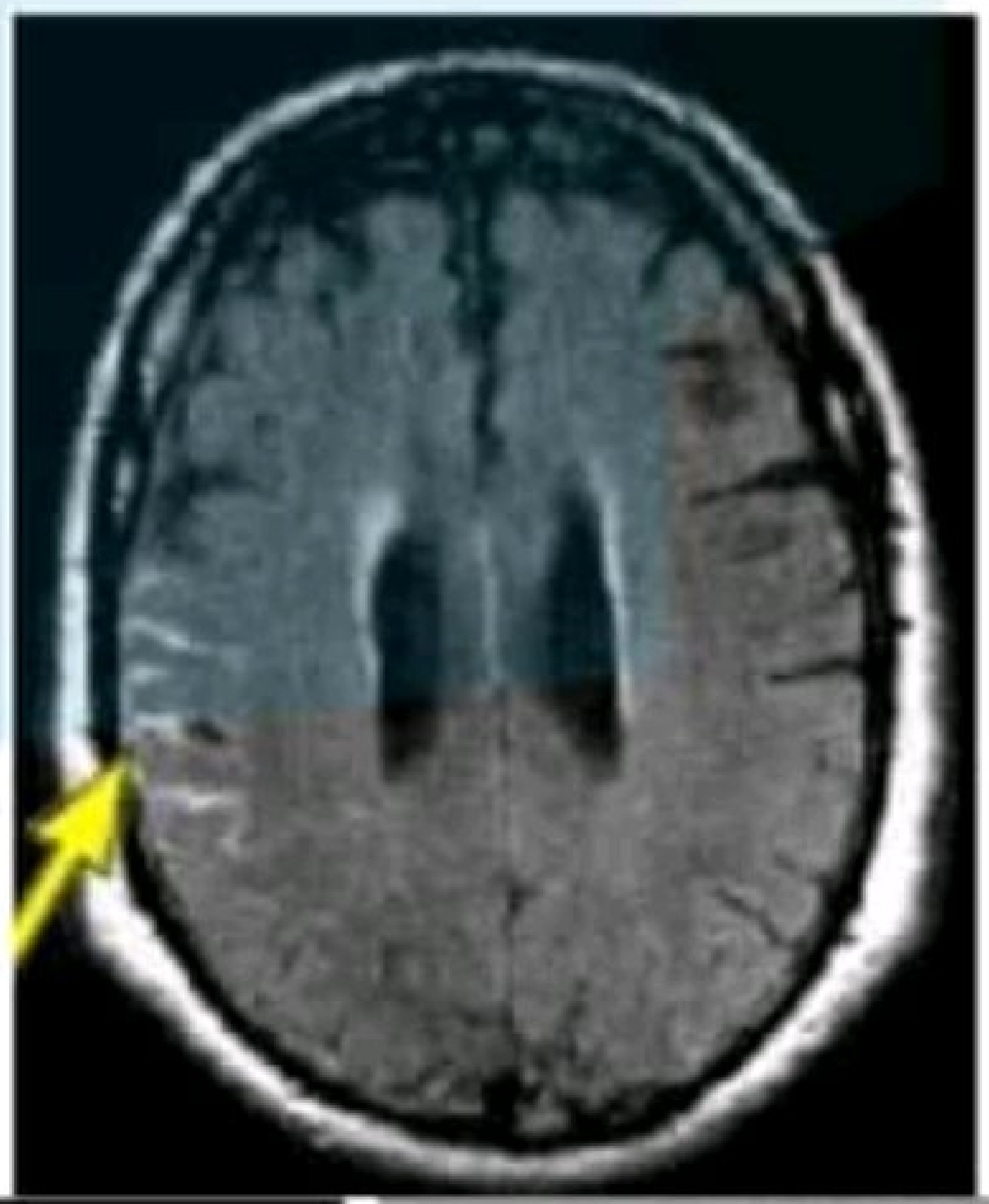

Malformation
Normal
Arteriovenous Malformation

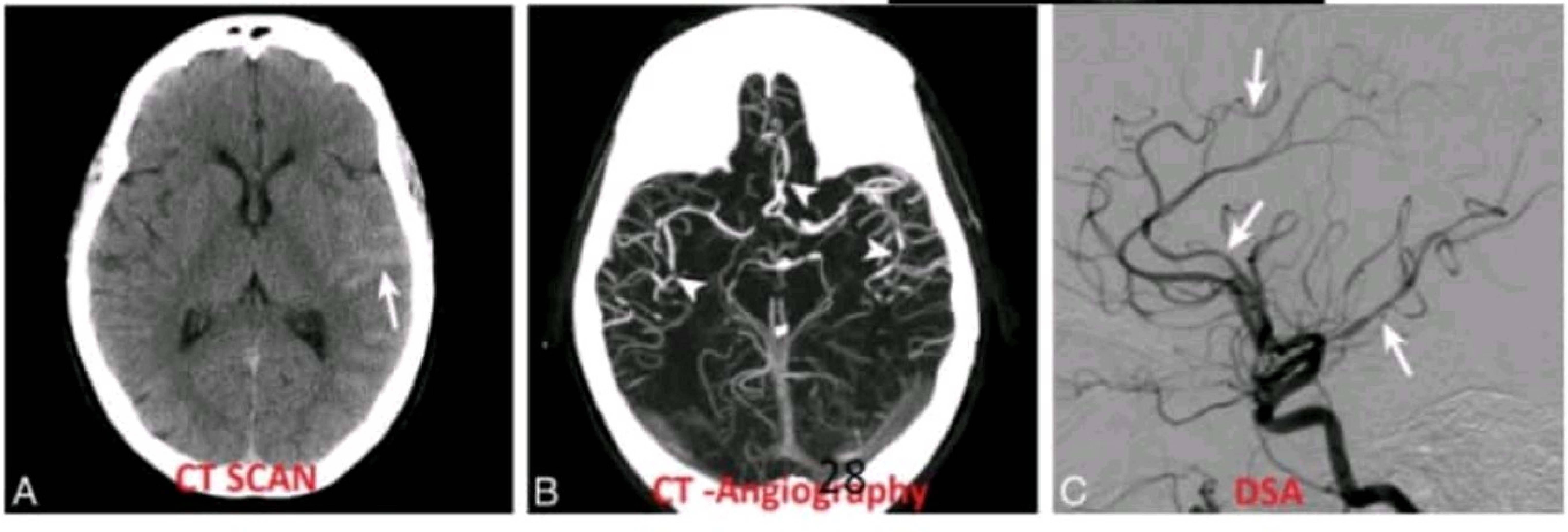

Pre-operative
Post-operative

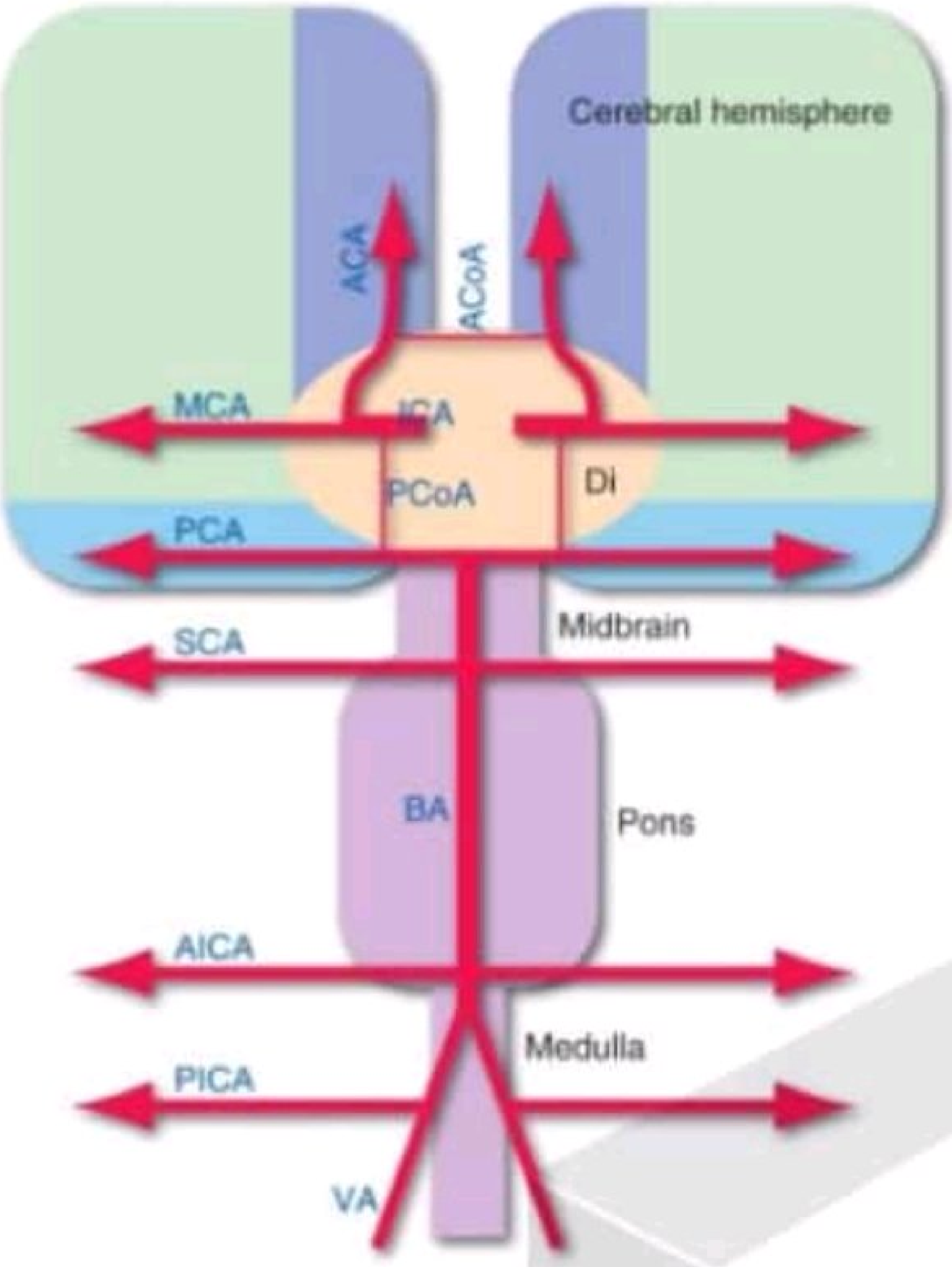
SUB-ARACHNOID HEMORRHAGE (SAH)

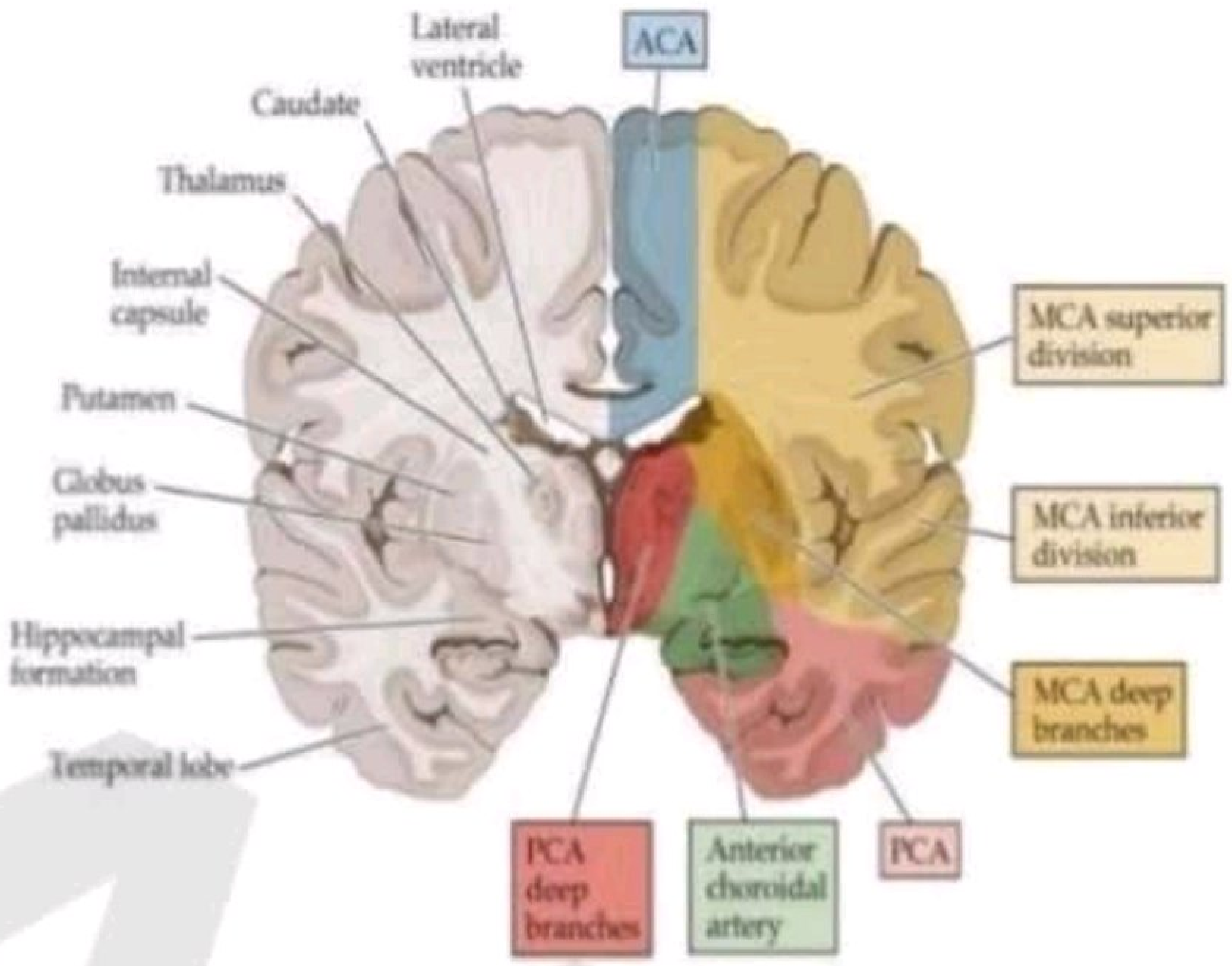
On MRI → The bleed is in sulci and Gyri

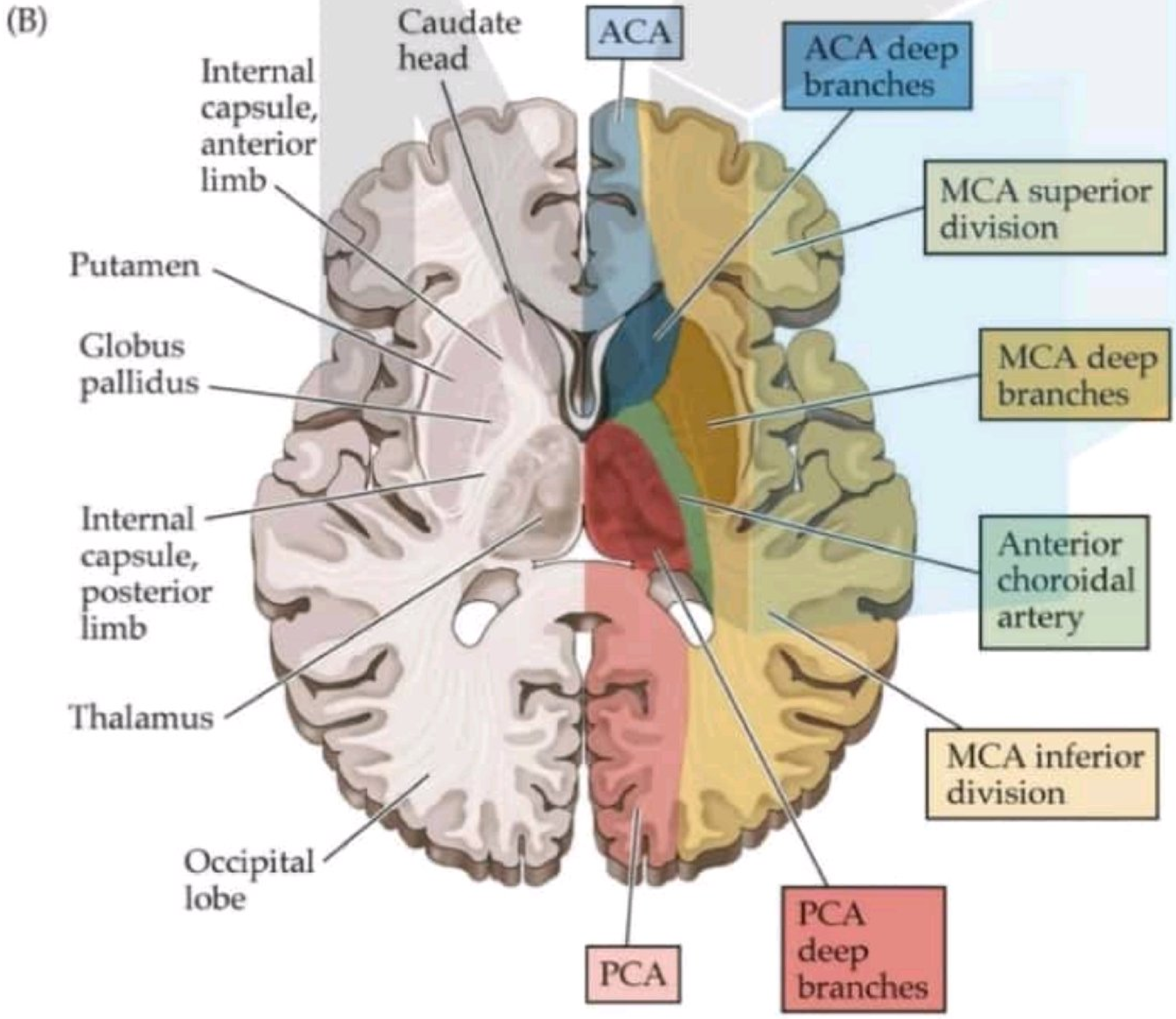
Lesion is localized via CT Angiography

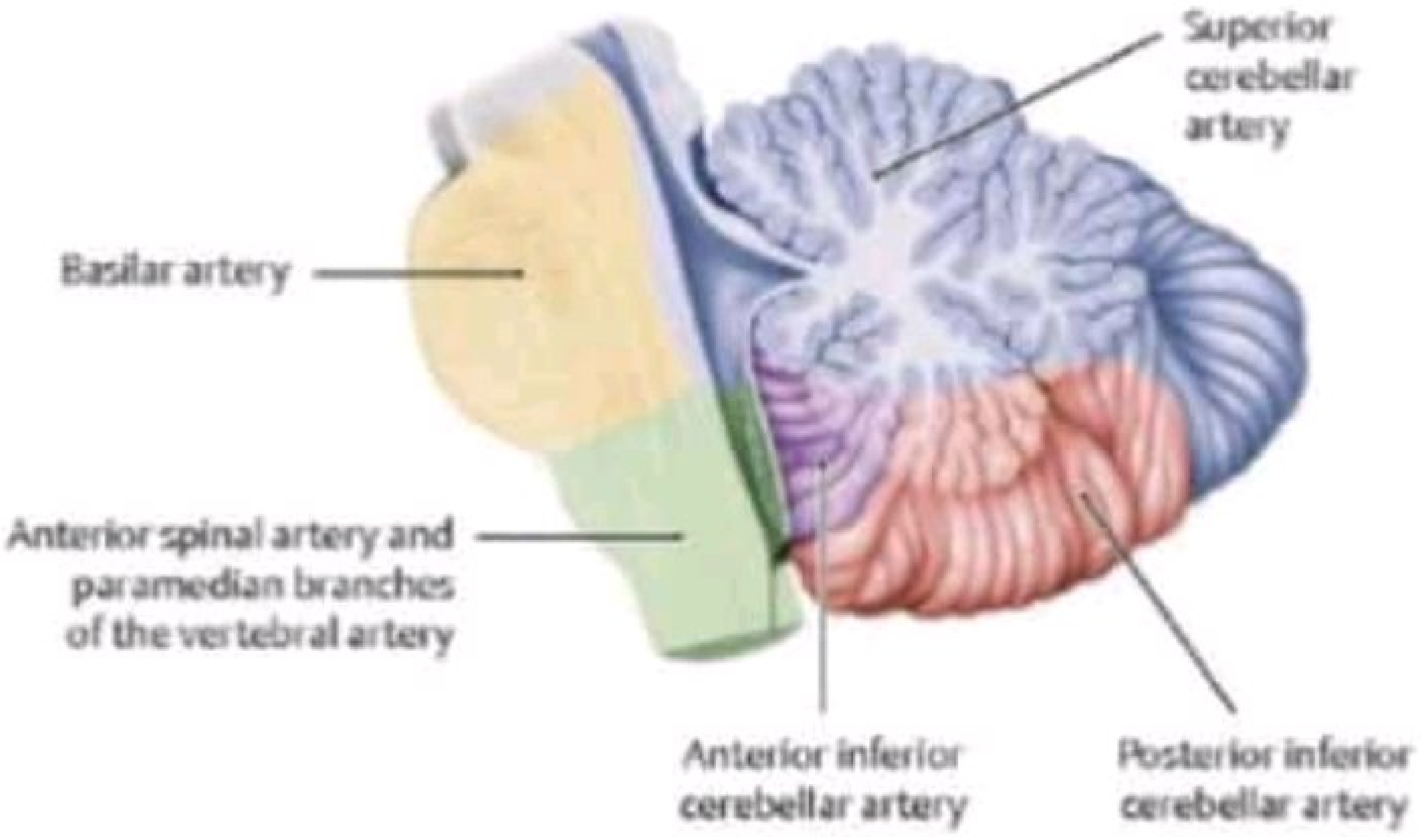


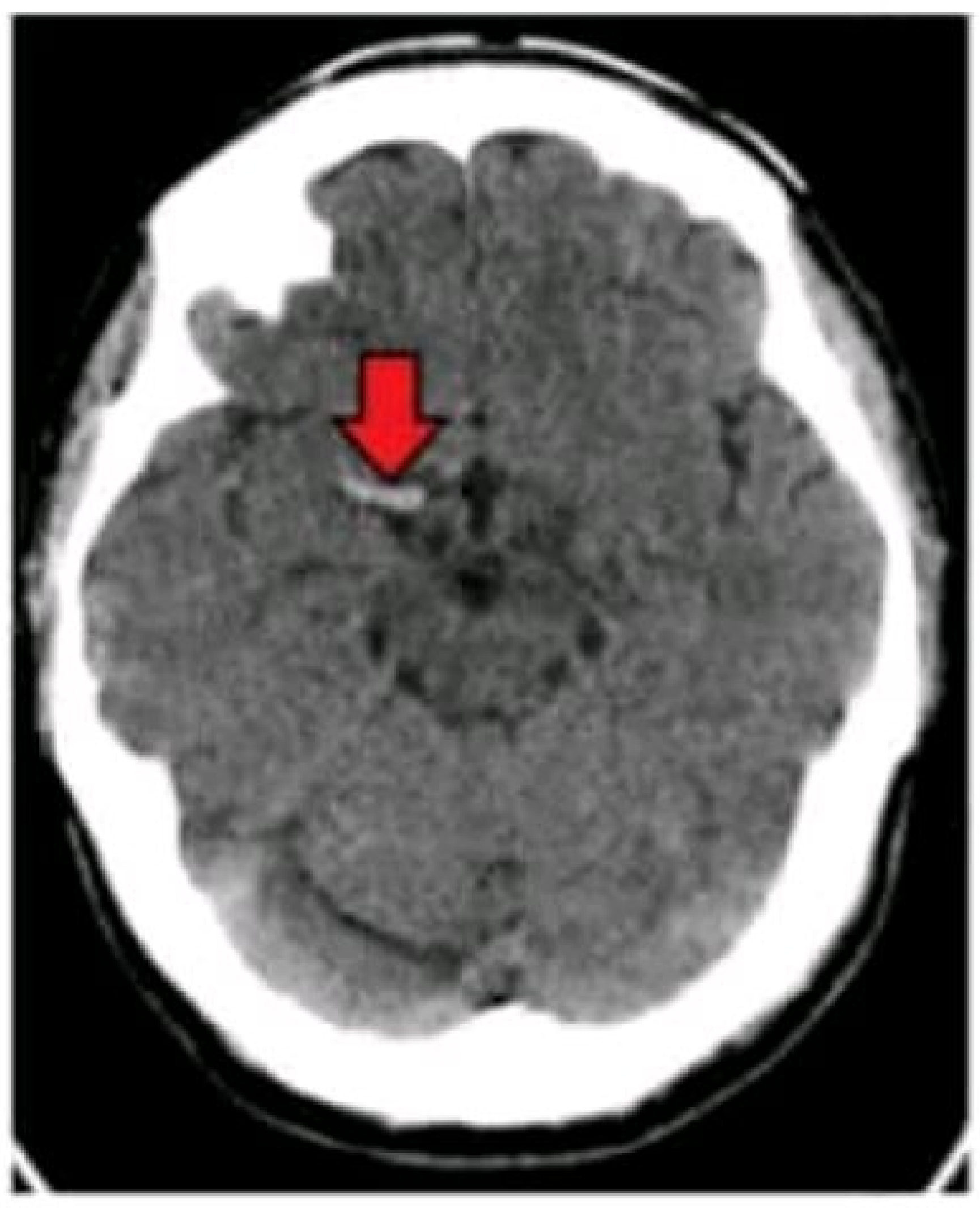

A
CT SCAN
B
CT -Angiography
C
DSA


Cerebral hemisphere
ACA
ACoA
MCA
ICA
PCoA
Di
PCA
SCA
Midbrain
BA
Pons
AICA
Medulla
PICA
VA


Lateral ventricle
ACA
Caudate
Thalamus
Internal capsule
MCA superior division
Putamen
Globus pallidus
MCA inferior division
Hippocampal formation
MCA deep branches
Temporal lobe
PCA deep branches
Anterior choroidal artery
PCA

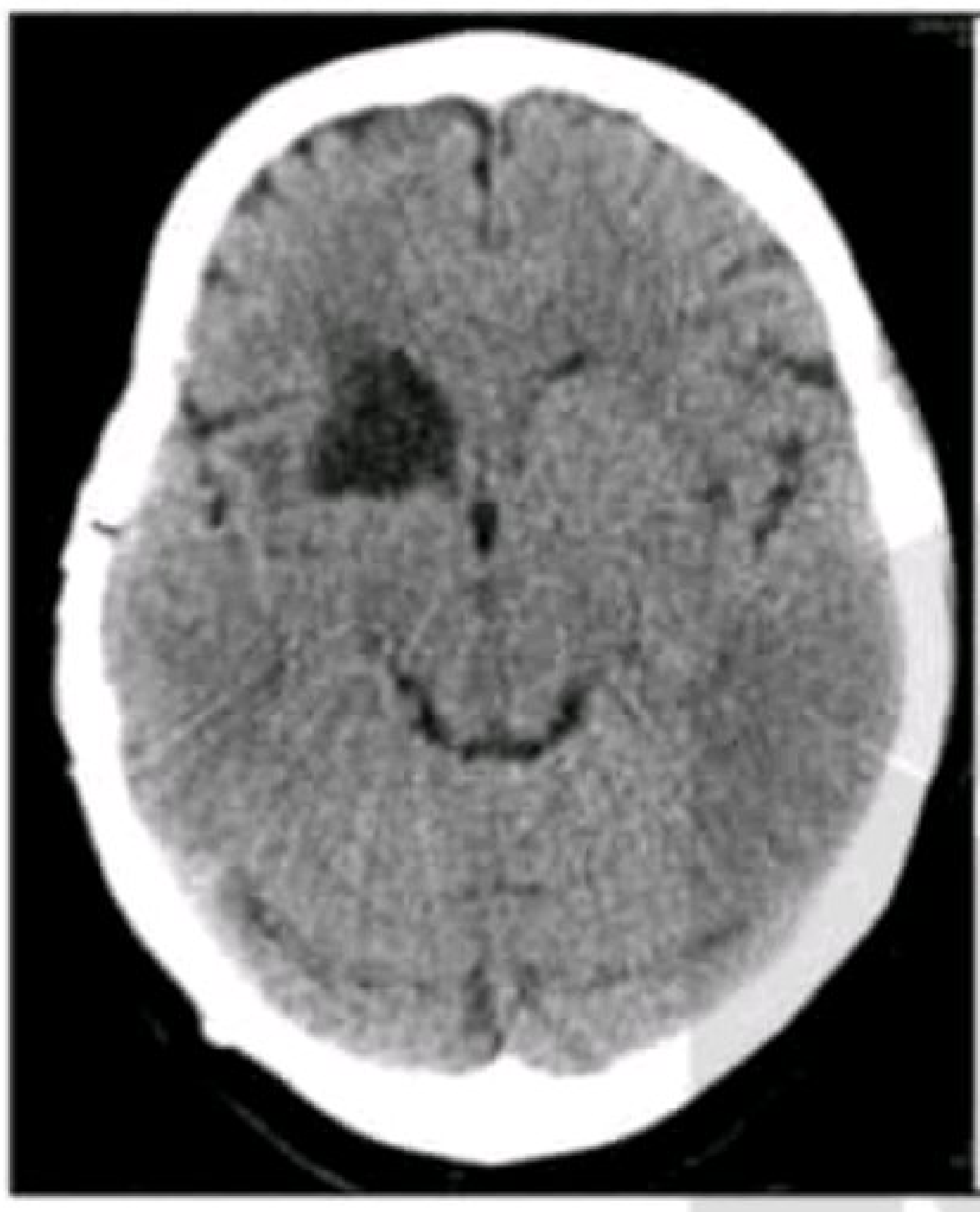

(B)
Caudate head
ACA
ACA deep branches
Internal capsule, anterior limb
MCA superior division
Putamen
Globus pallidus
MCA deep branches
Internal capsule, posterior limb
Anterior choroidal artery
Thalamus
MCA inferior division
Occipital lobe
PCA
PCA deep branches


Superior cerebellar artery
Basilar artery
Anterior spinal artery and paramedian branches of the vertebral artery
Anterior inferior cerebellar artery
Posterior inferior cerebellar artery

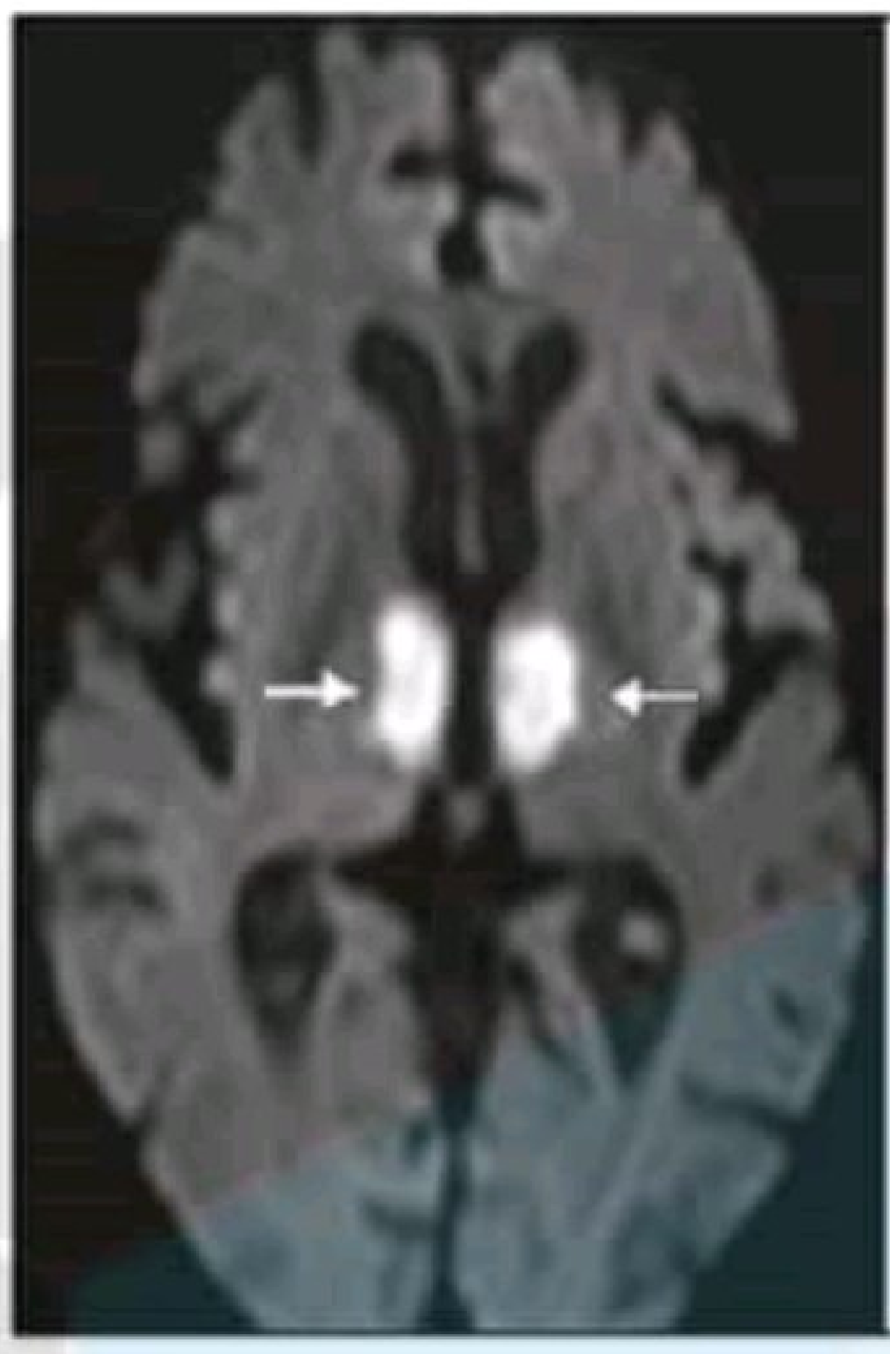


FIRST SIGN OF INFARCT ON CT

DENSE MCA SIGN



INFARCT OF ARTERY OF HEUBNER

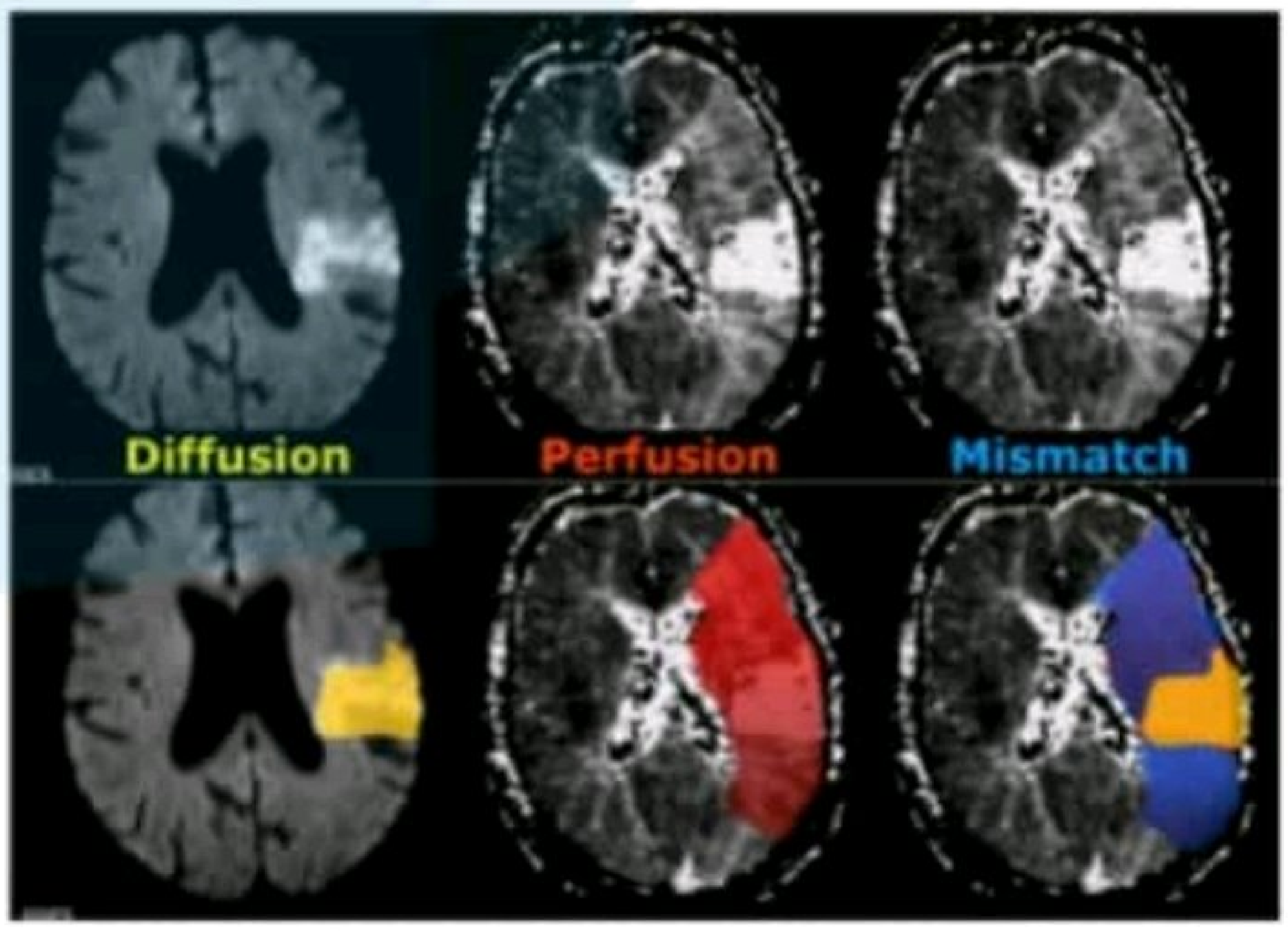


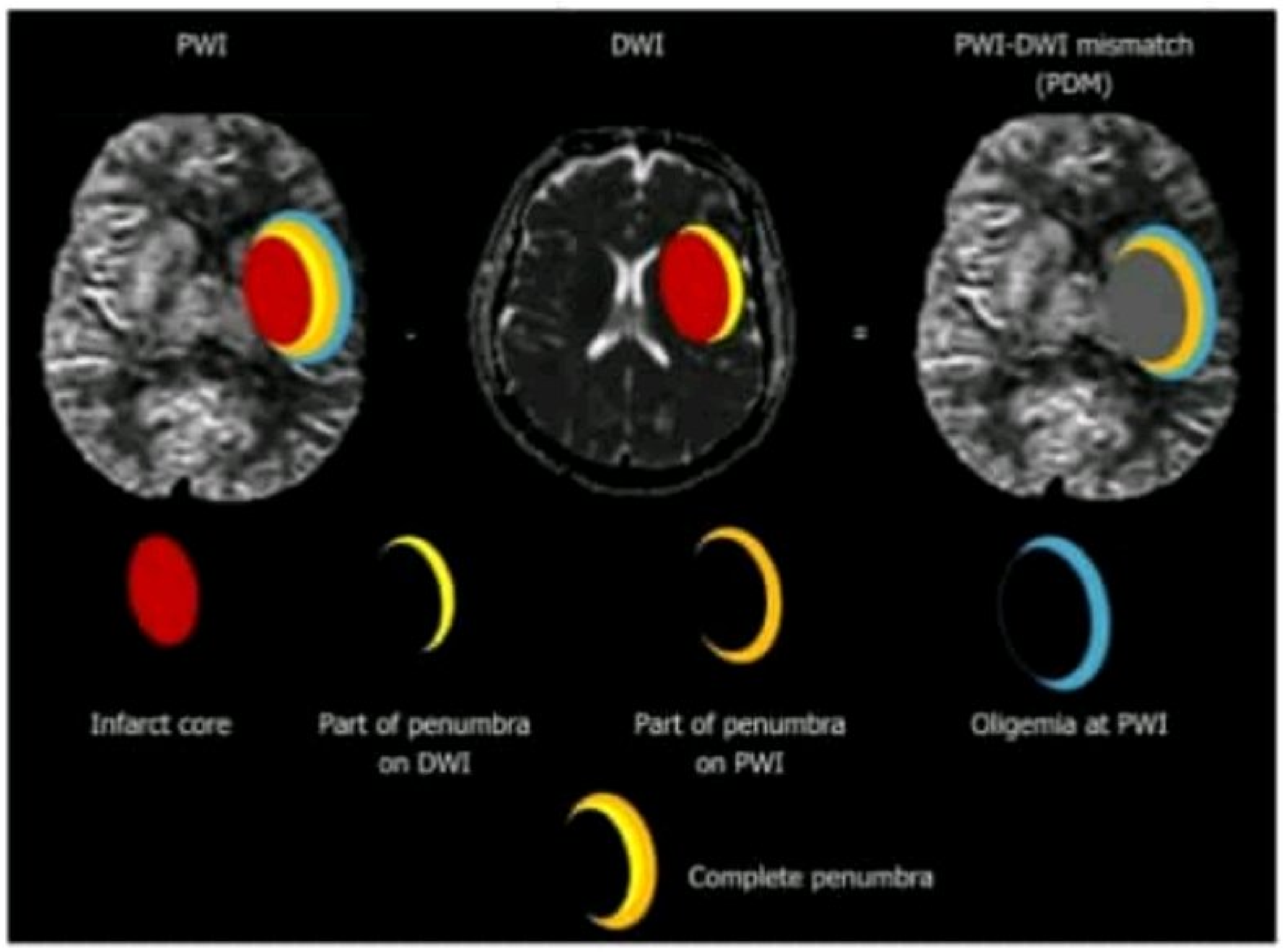
INFARCT OF ARTERY OF PERCHERON (Anatomical Variant of PCA)

Q. Brain Hemorrhage is earliest seen on → Diffusion weighted MRI (3-30 mins)

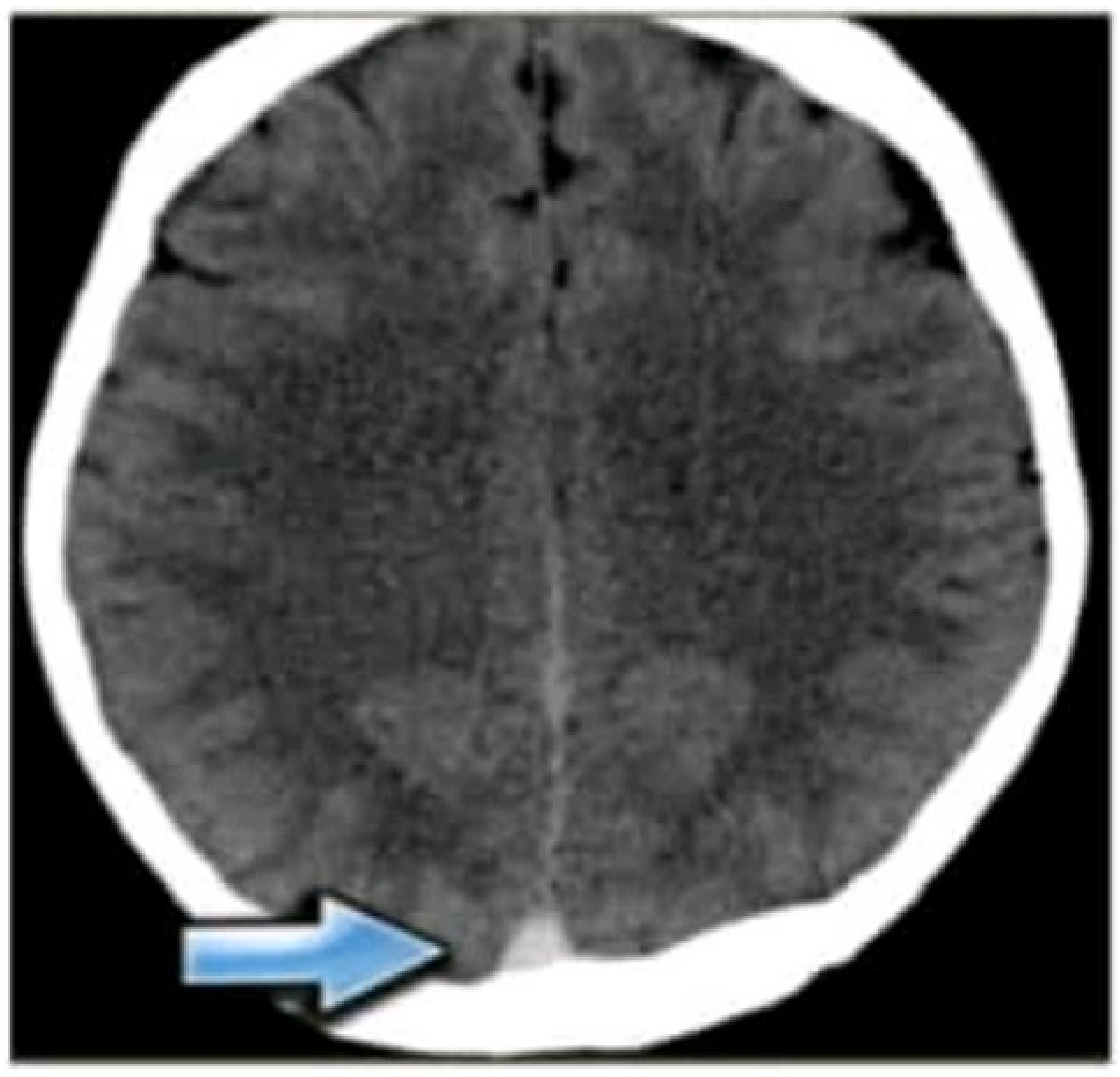
There is a mismatch between the areas of infarct seen on Diffusion Weighted MRI and Perfusion weighted MRI.

The area of mismatch is called as PENUMBRA which is aimed to be saved by in-time thrombolytic therapy.


Diffusion
Perfusion
Mismatch


PWI
DWI
PWI-DWI mismatch (PDM)
-
=
Infarct core
Part of penumbra on DWI
Part of penumbra on PWI
Oligemia at PWI
Complete penumbra

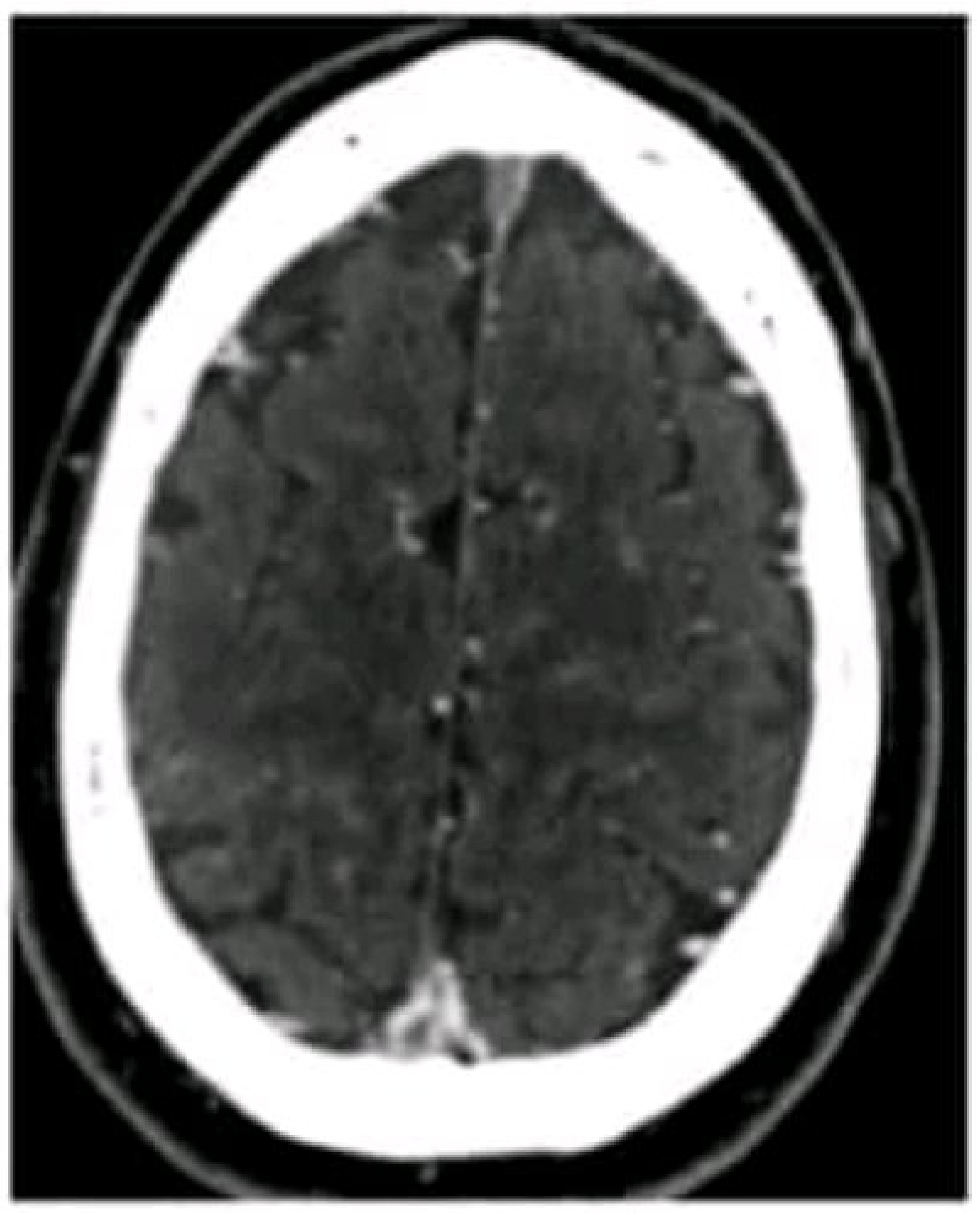
CEREBRAL VENOUS THROMBOSIS



NCCT shows DELTA sign

This venous thrombosis can be seen in hypercoagulable states like Pregnancy, Protein C/S Deficiency, Dehydration

CECT shows EMPTY DELTA Sign



BRAIN STEM SYNDROMES

Blood supply to MEDULLA:

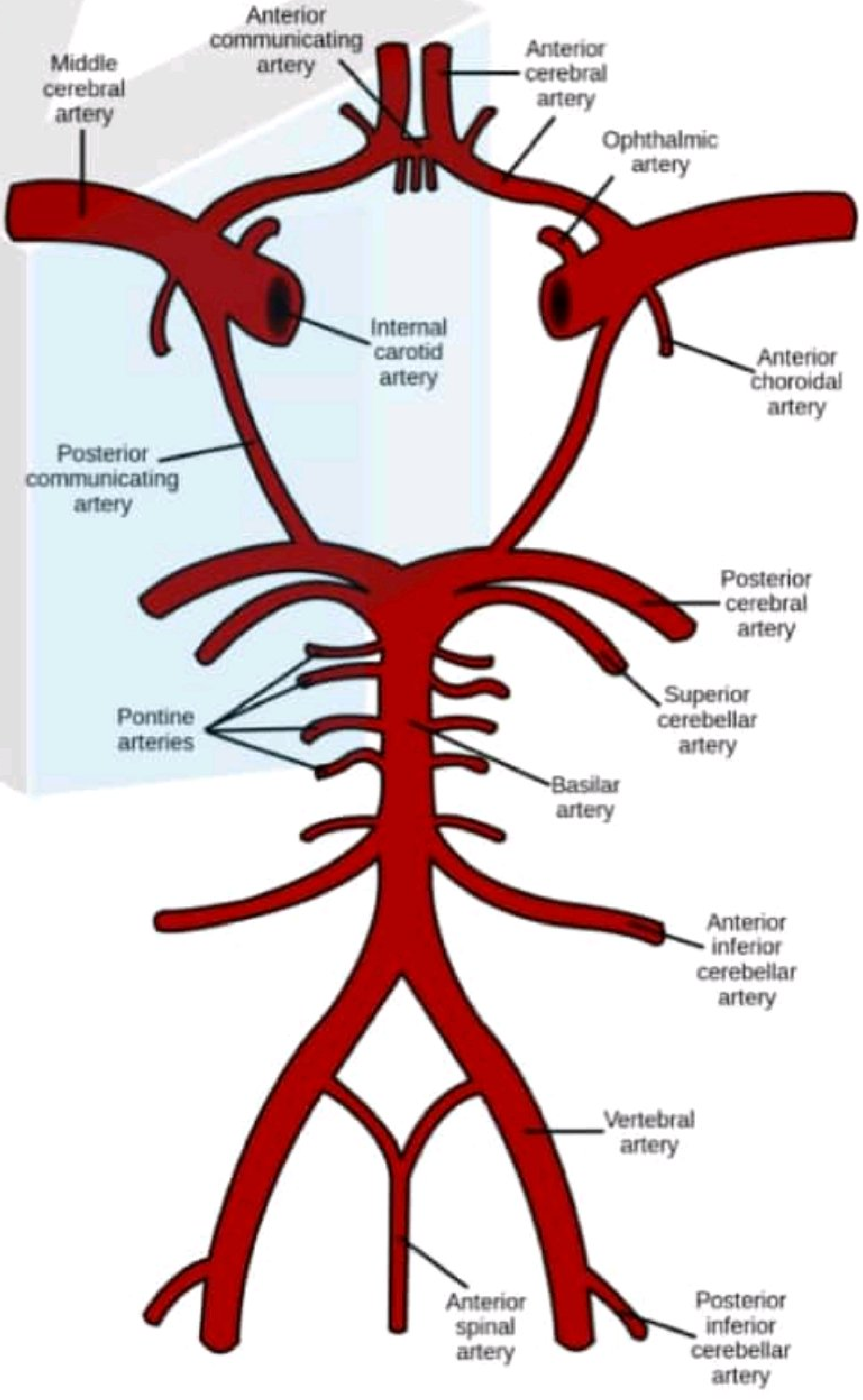
- Basilar Artery
- Posterior Spinal Artery
- PICA
- Vertebral Artery
- Anterior Spinal Artery

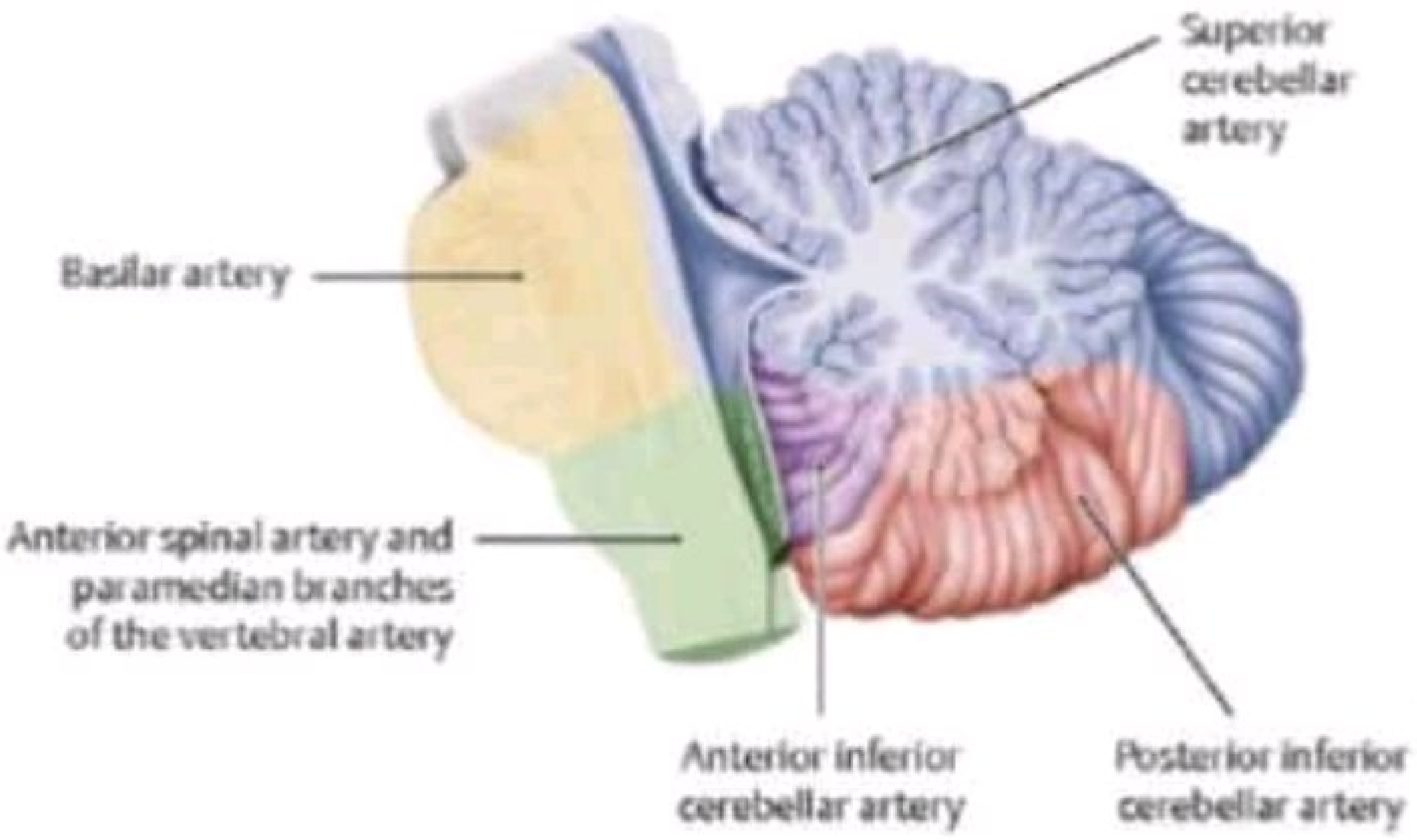
Blood supply to PONS:

- AICA
- Basilar Artery
- Superior Cerebellar Artery

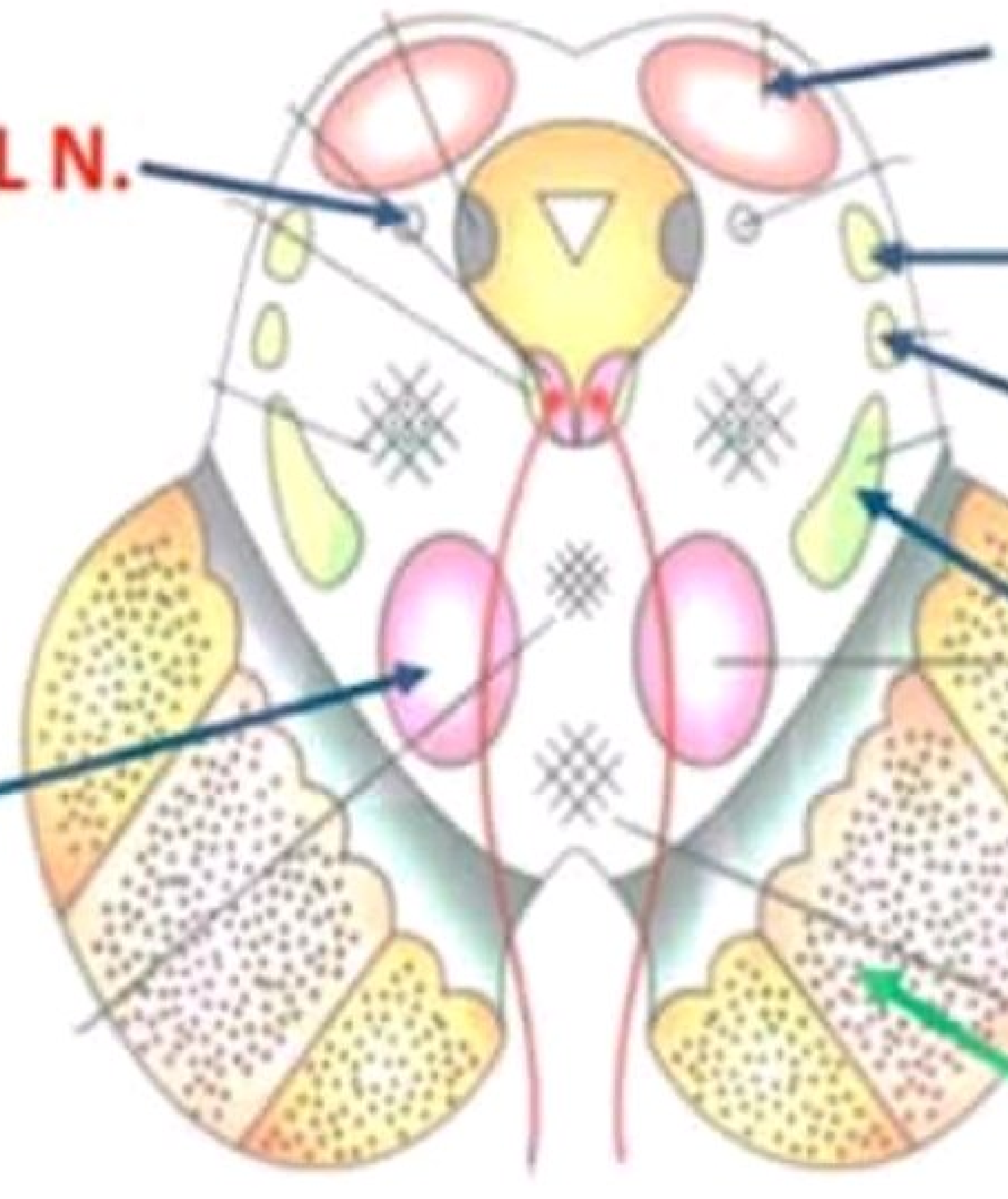
Blood supply to MIDBRAIN:

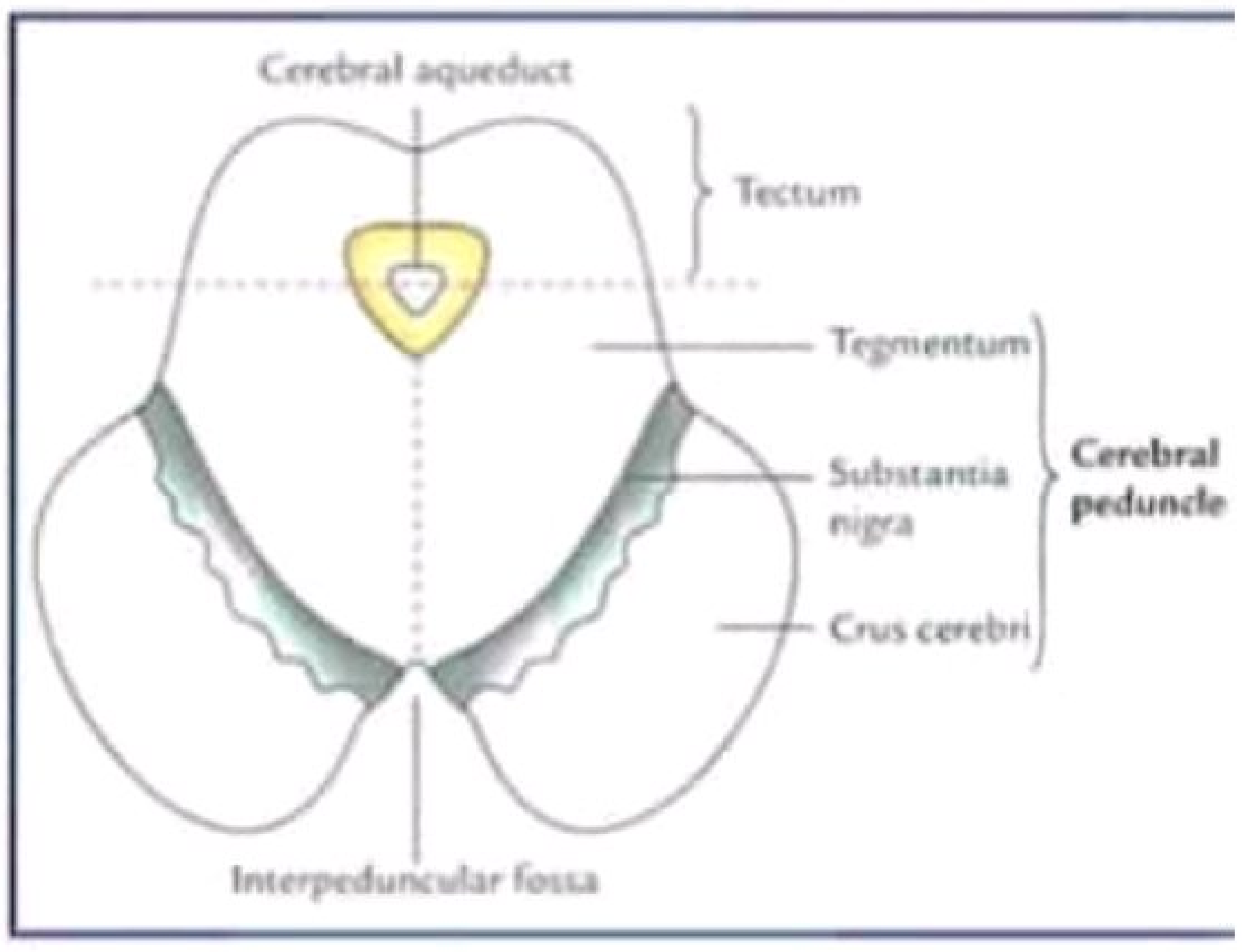
- Posterior Cerebral Artery
- Basilar Artery
- Posterior Cerebellar Artery


Anterior communicating artery
Middle cerebral artery
Anterior cerebral artery
Ophthalmic artery
Internal carotid artery
Anterior choroidal artery
Posterior communicating artery
Posterior cerebral artery
Superior cerebellar artery
Pontine arteries
Basilar artery
Anterior inferior cerebellar artery
Vertebral artery
Anterior spinal artery
Posterior inferior cerebellar artery

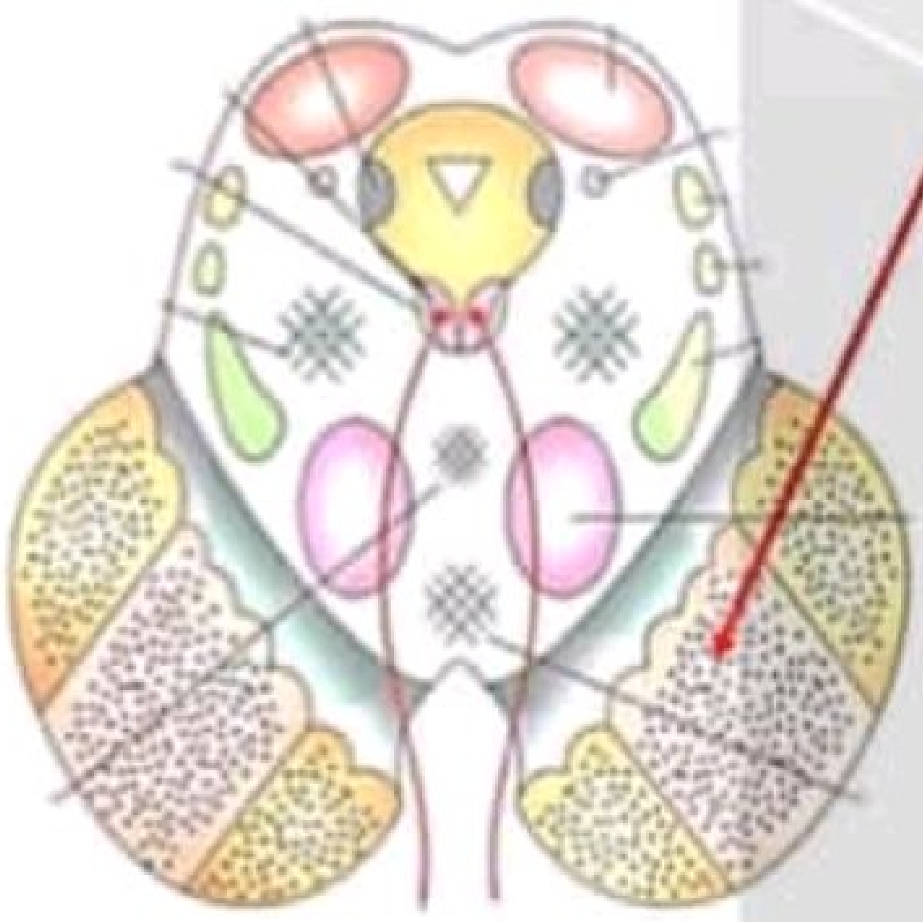

Superior cerebellar artery
Basilar artery
Anterior spinal artery and paramedian branches of the vertebral artery
Anterior inferior cerebellar artery
Posterior inferior cerebellar artery

MIDBRAIN

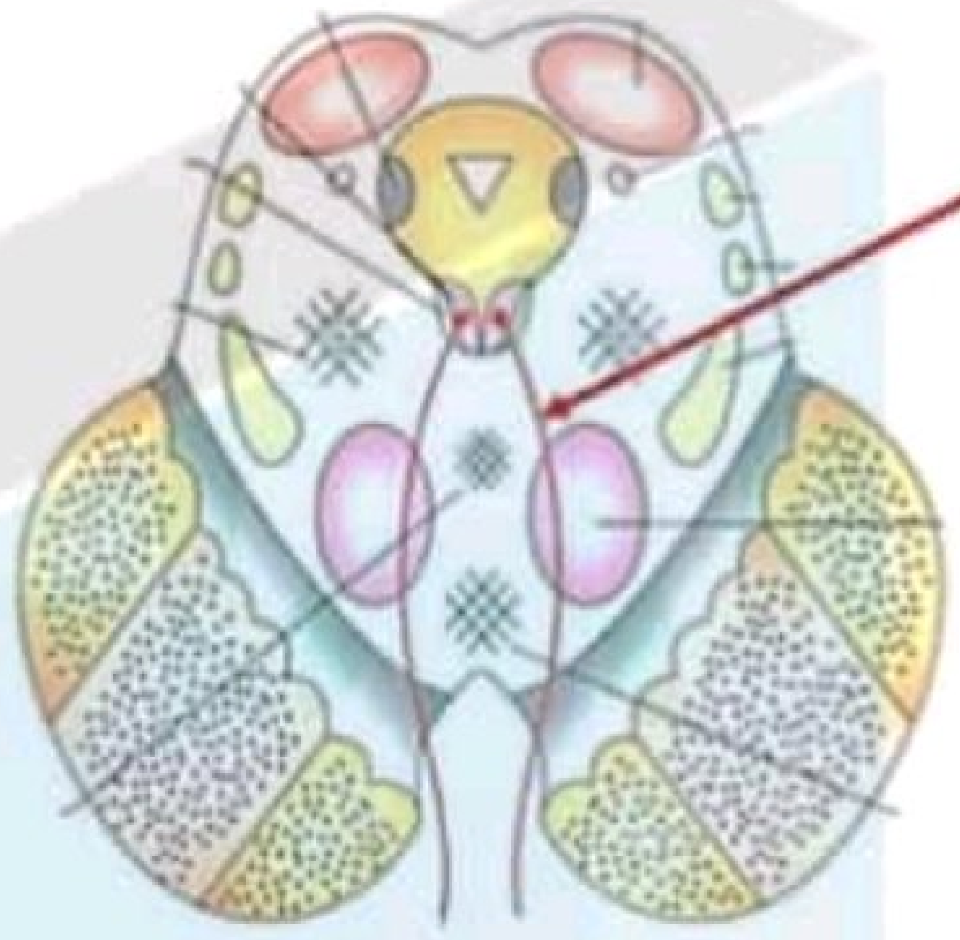

SUP. COLLICULUS
PRETECTAL N.
SPINAL LEMNISCUS
TRIGEMINAL LEMNISCUS
MEDIAL LEMNISCUS
RED N.
CORTICOSPINAL TRACT IN CRUS CEREBRI


Cerebral aqueduct
Tectum
Tegmentum
Substantia nigra
Crus cerebri
Cerebral peduncle
Interpeduncular fossa

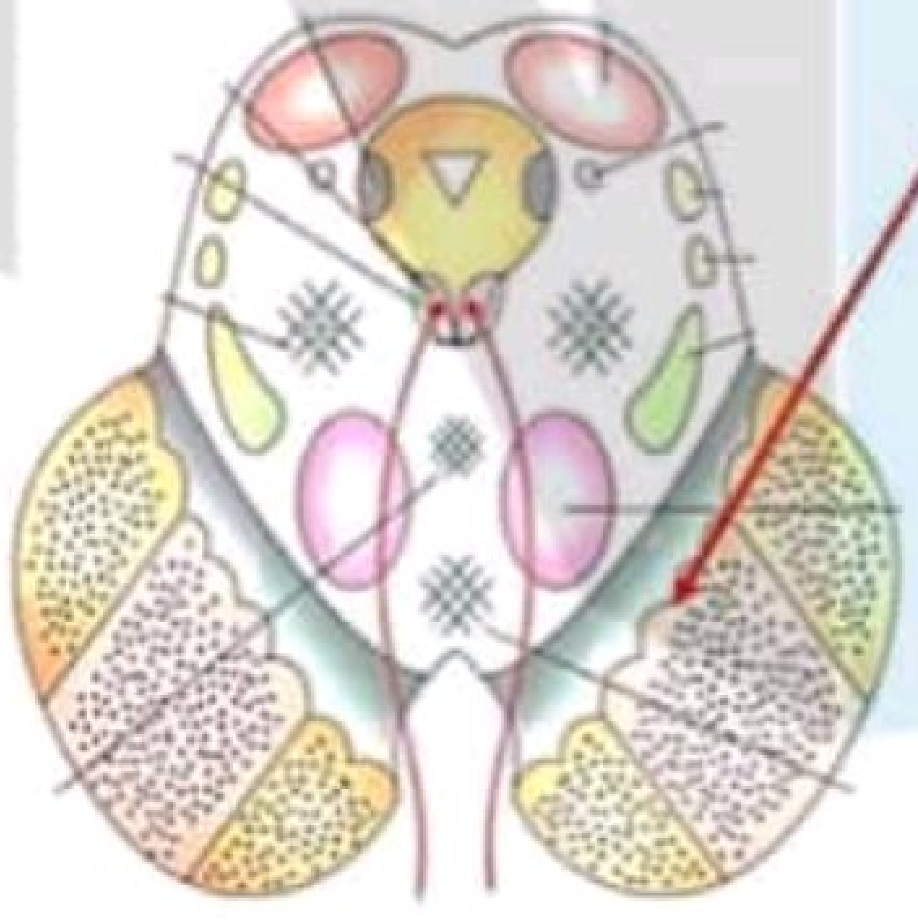
WEBER'S SYNDROME


corticospinal tract in the crus cerebri

Contralateral hemiplegia

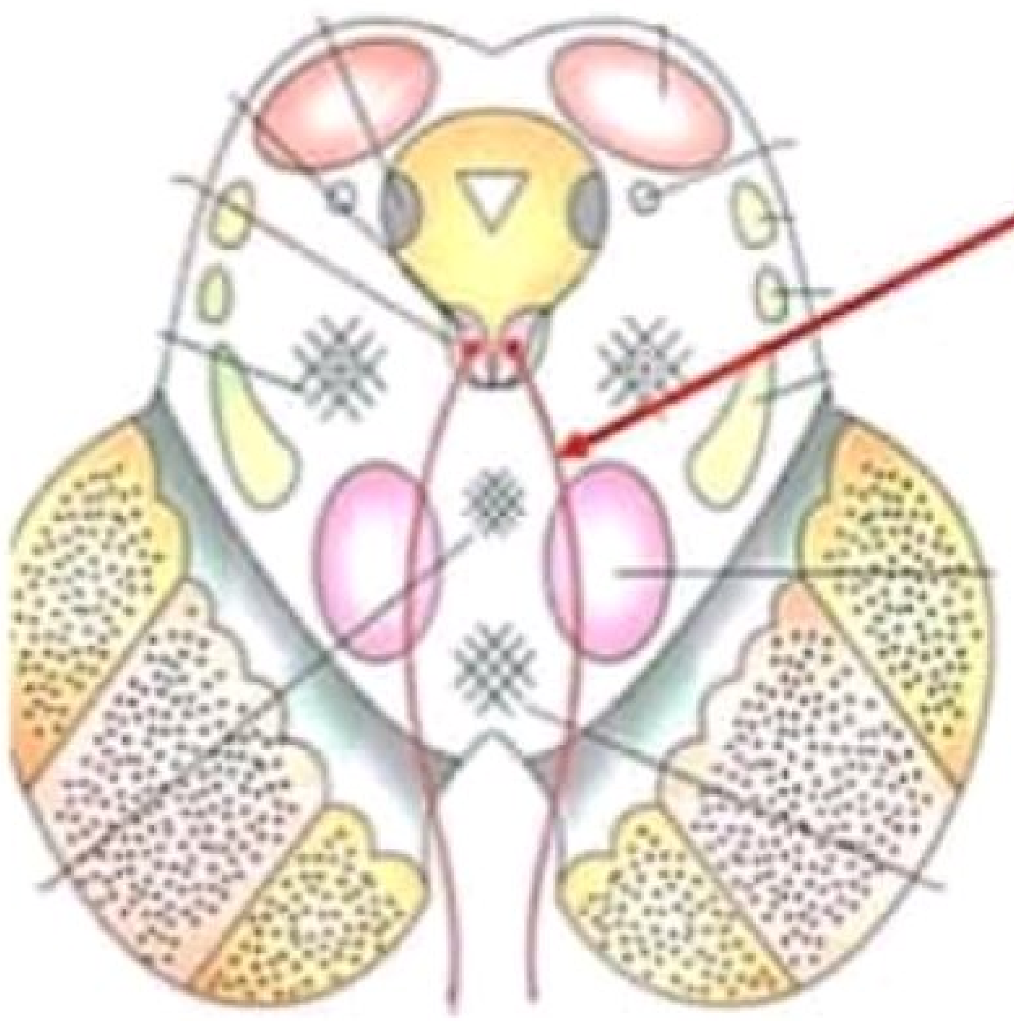

3RD CRANIAL NERVE

PTOSIS
EYE – DOWN & OUT
PUPIL – DILATED & FIXED

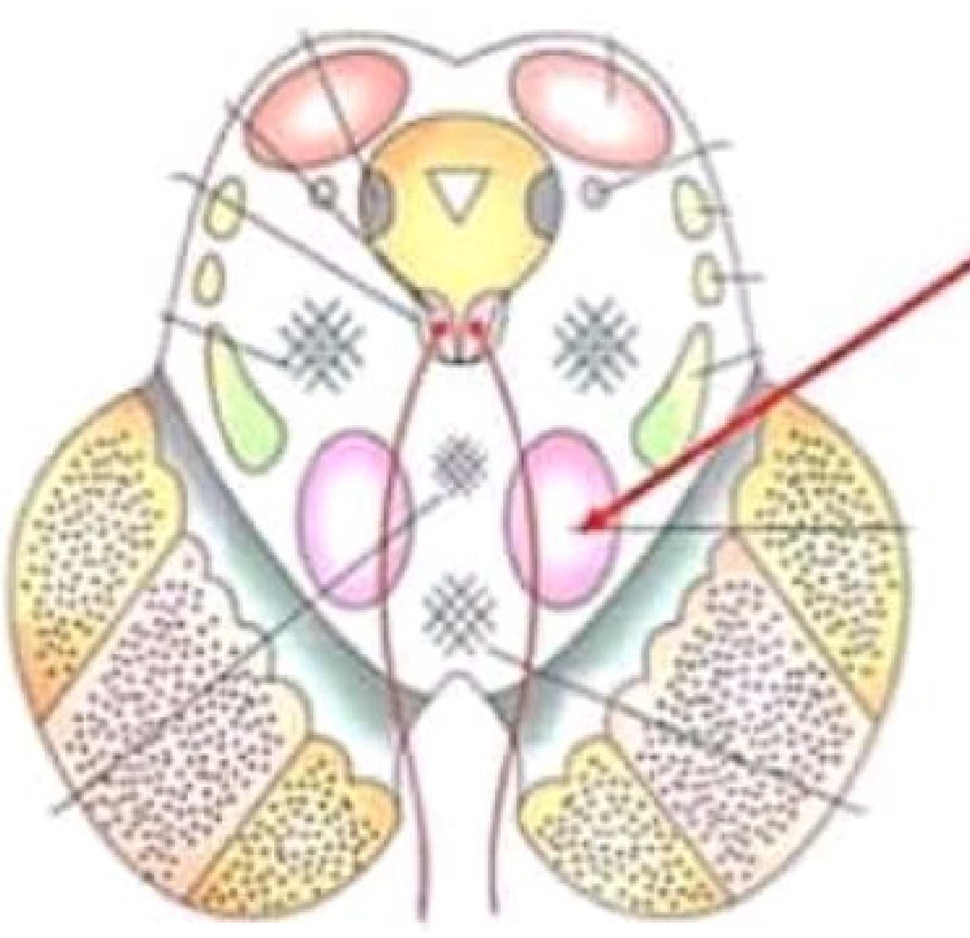

corticobulbar tract in the crus cerebri

Contralateral paralysis of the lower part of the face & tongue

CLAUDE'S SYNDROME


3RD CRANIAL NERVE

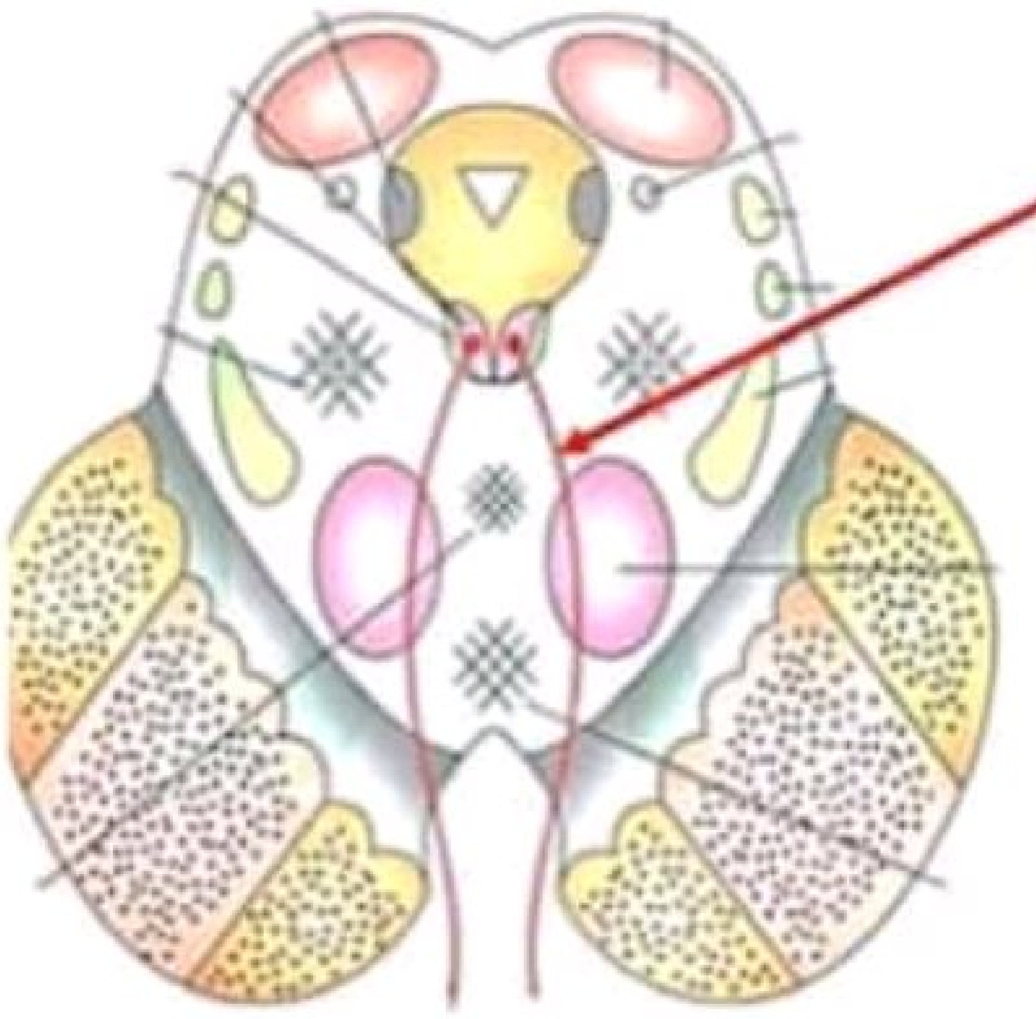
PTOSIS
EYE – DOWN & OUT
PUPIL – DILATED & FIXED


RED NUCLEUS

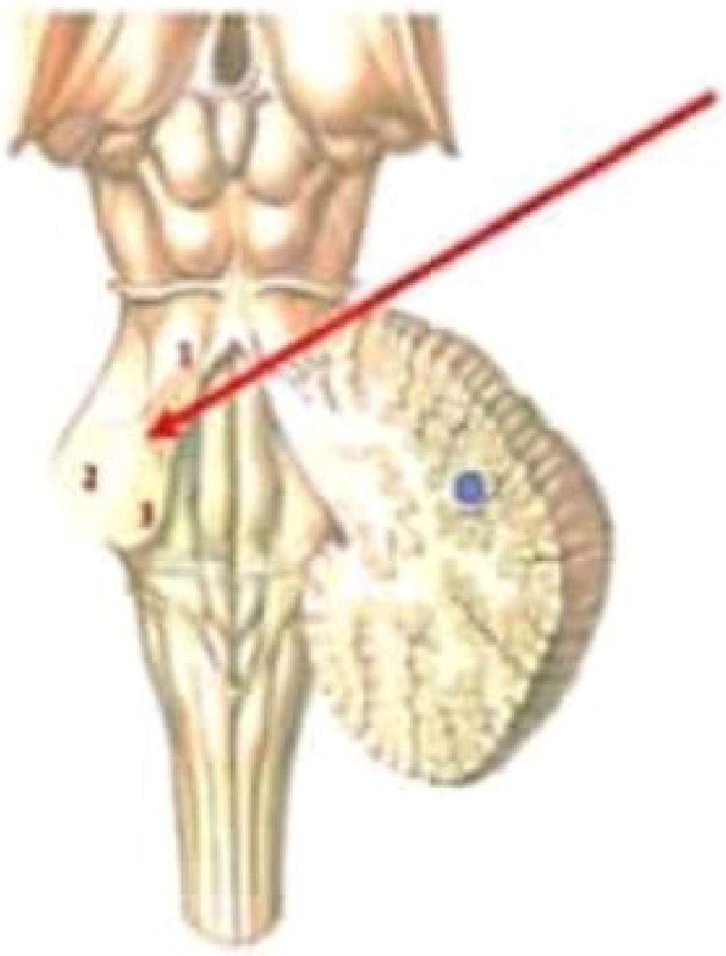
CONTRALATERAL TREMOR, ATAXIA

BENEDIKT'S SYNDROME = WEBERS + CLAUDES

NOTHNAGEL'S SYNDROME

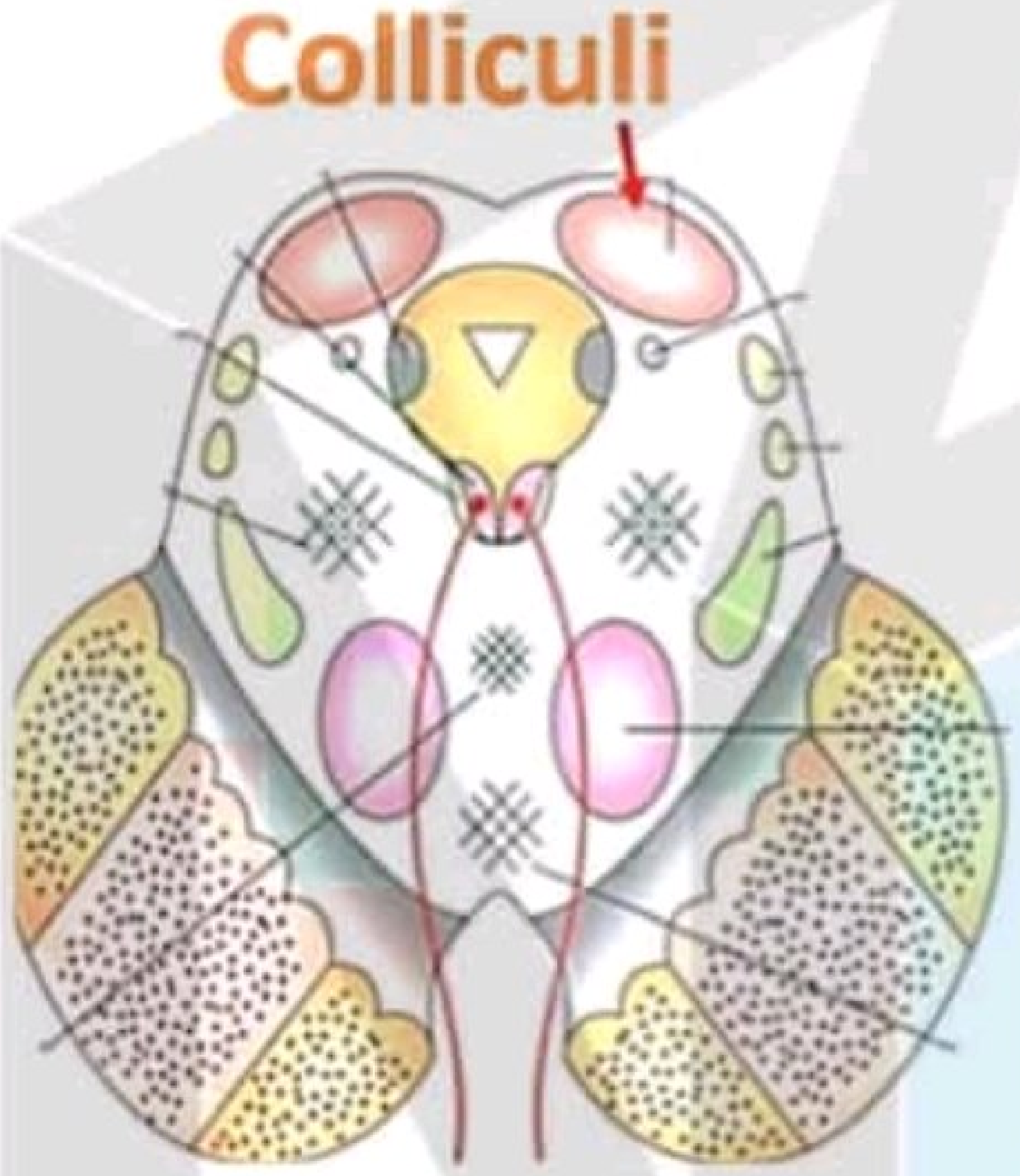

3RD CRANIAL NERVE

PTOSIS
EYE – DOWN & OUT
PUPIL – DILATED & FIXED


Cerebellar peduncle
1- superior cerebellar peduncle
2- middle cerebellar peduncle
3- inferior cerebellar peduncle
1
2
3
SUPERIOR CEREBELLAR PEDUNCLE

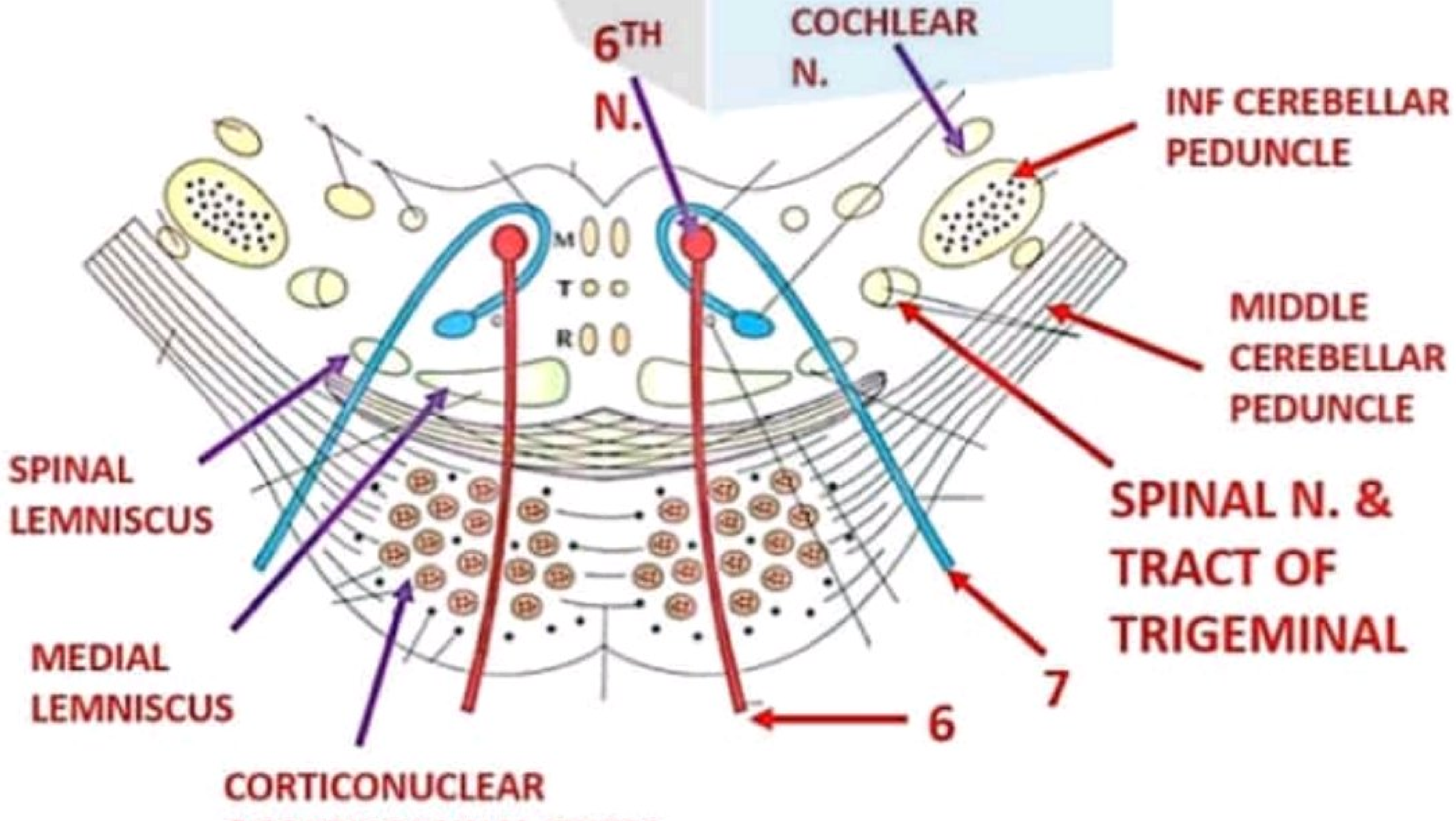
ATAXIA ONLY

PERINAUD'S SYNDROME

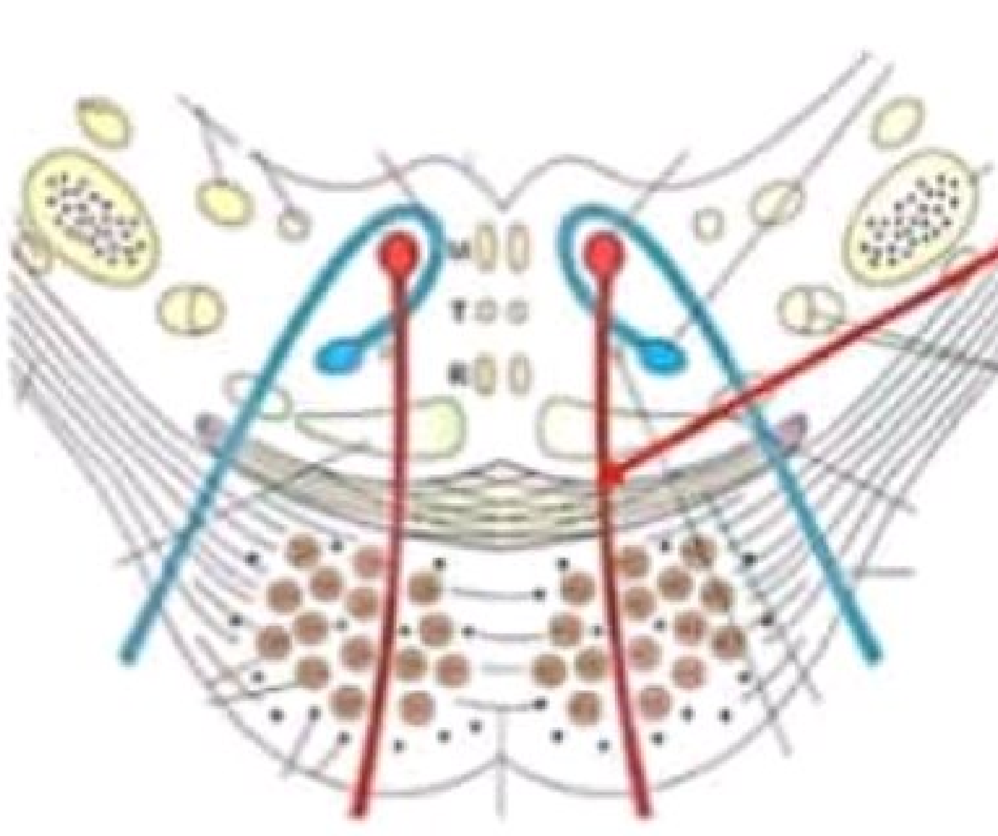


- loss of upward gaze
- ARP
- CONVERGENCE RETRACTION NYSTAGMUS
- LID RETRACTION (COLLIER'S SIGN)

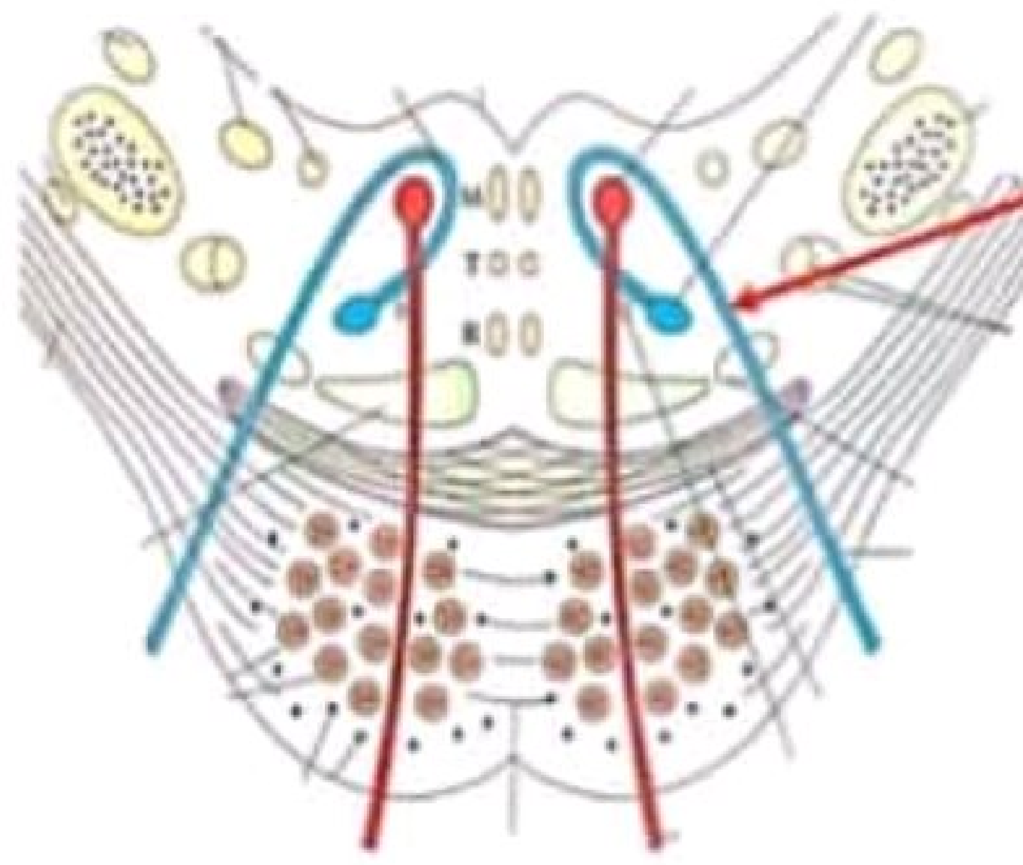
PONS


6TH N.
COCHLEAR N.
INF CEREBELLAR PEDUNCLE
M
T
R
MIDDLE CEREBELLAR PEDUNCLE
SPINAL LEMNISCUS
SPINAL N. & TRACT OF TRIGEMINAL
MEDIAL LEMNISCUS
7
6
CORTICONUCLEAR &CORTICOSPINAL FIBRES

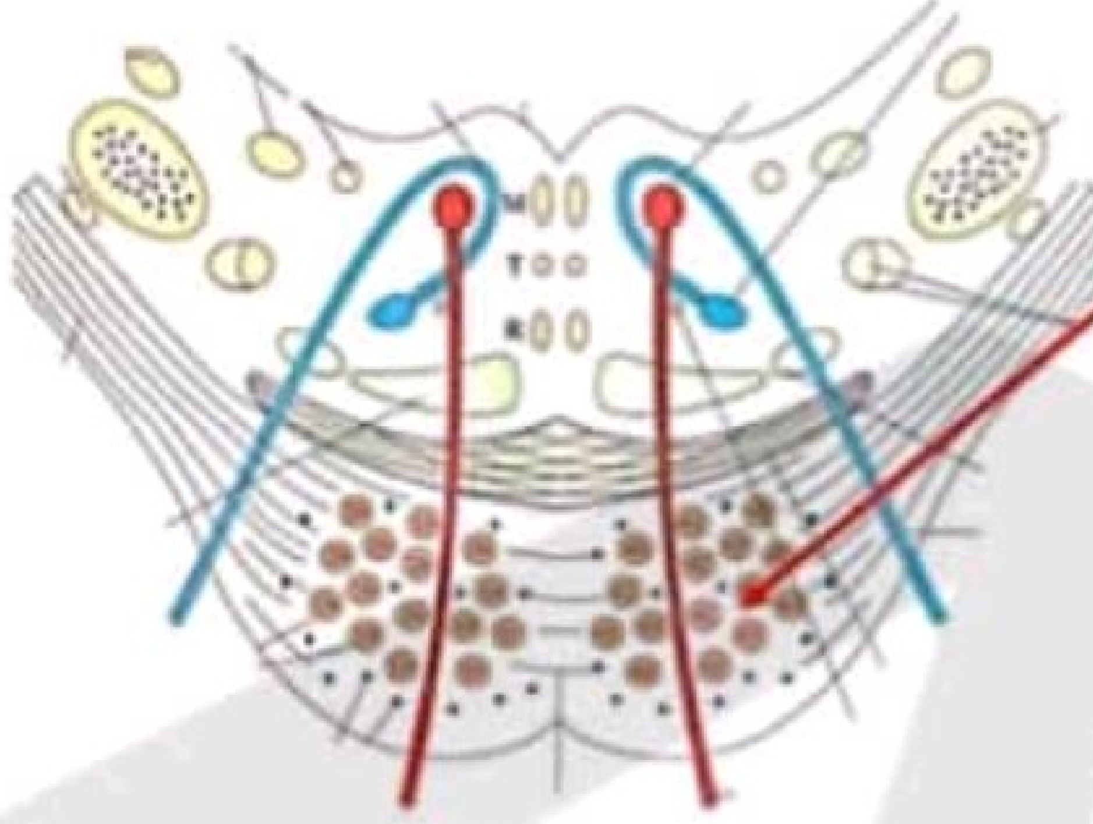
MILLARD GUBLER SYNDROME



MEDIAL SQUINT

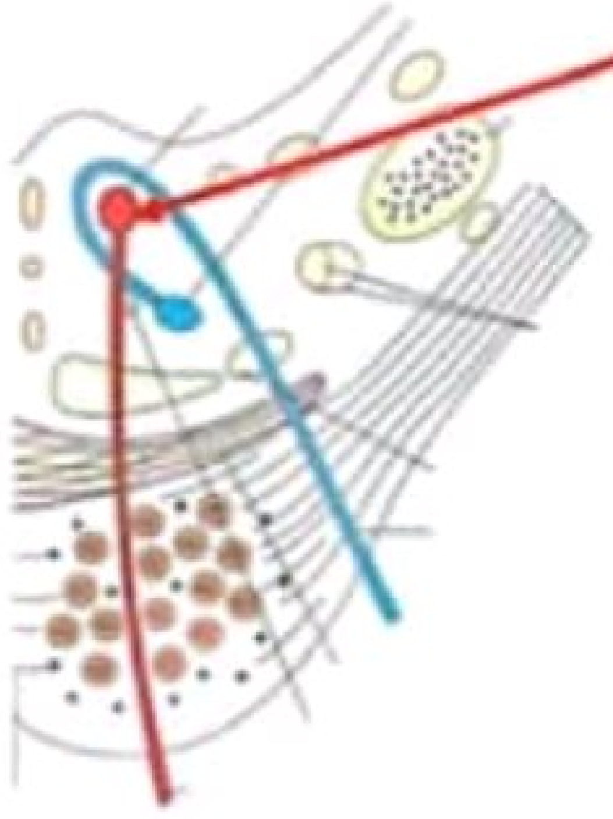


FACIAL PALSY

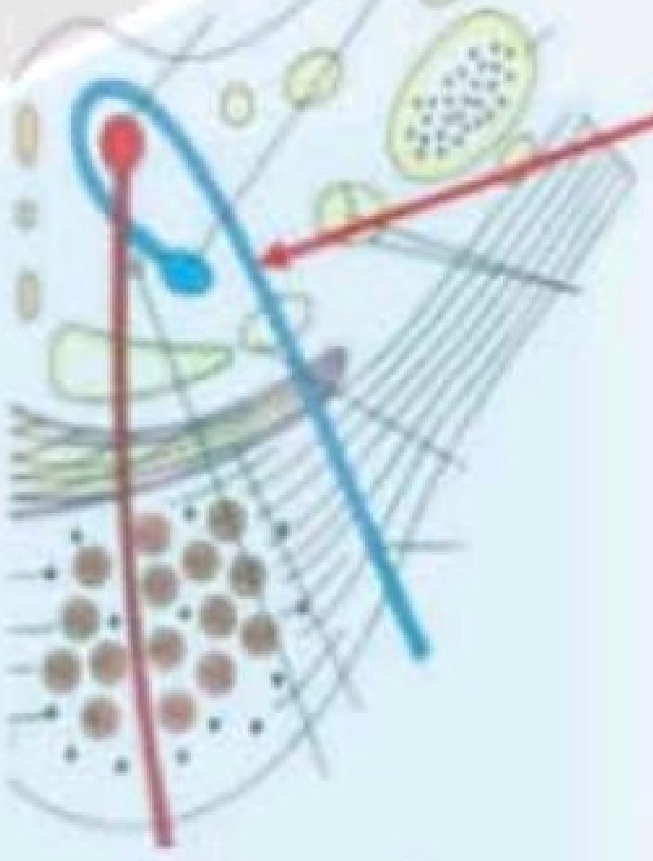

Corticospinal tract

Contralateral hemiplegia

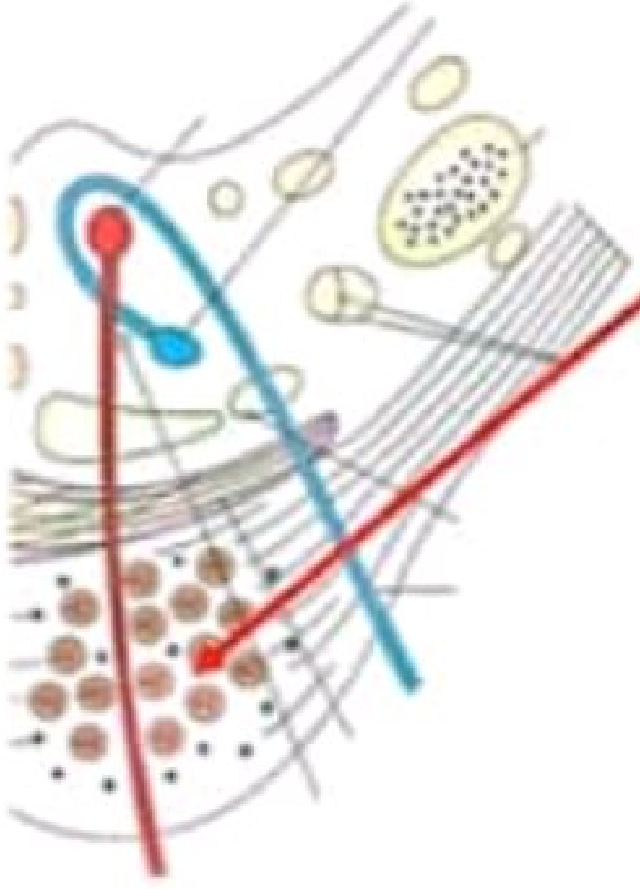
FOVILLE SYNDROME


6TH nerve NUCLEUS

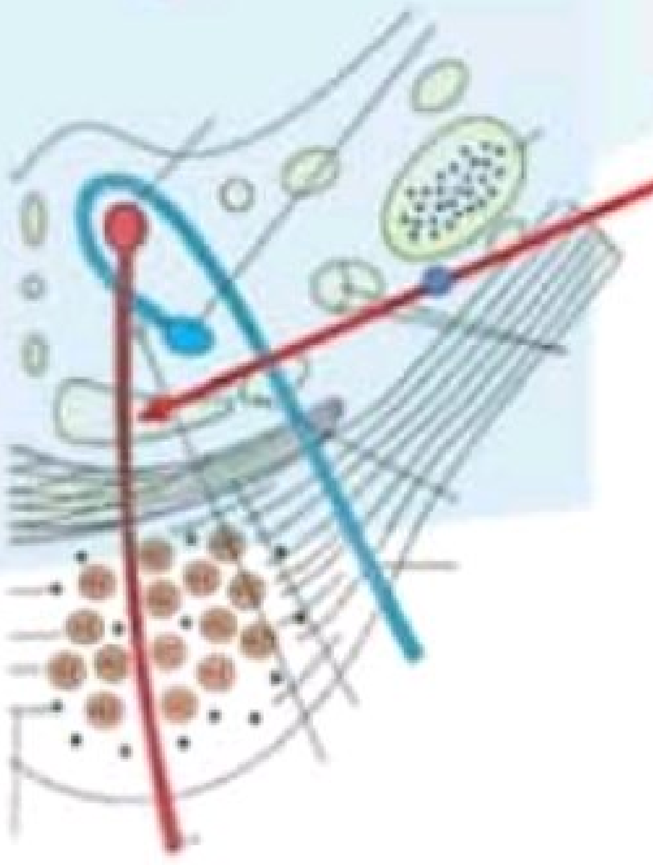
- Medial Squint
- Lateral Gaze palsy



FACIAL PALSY

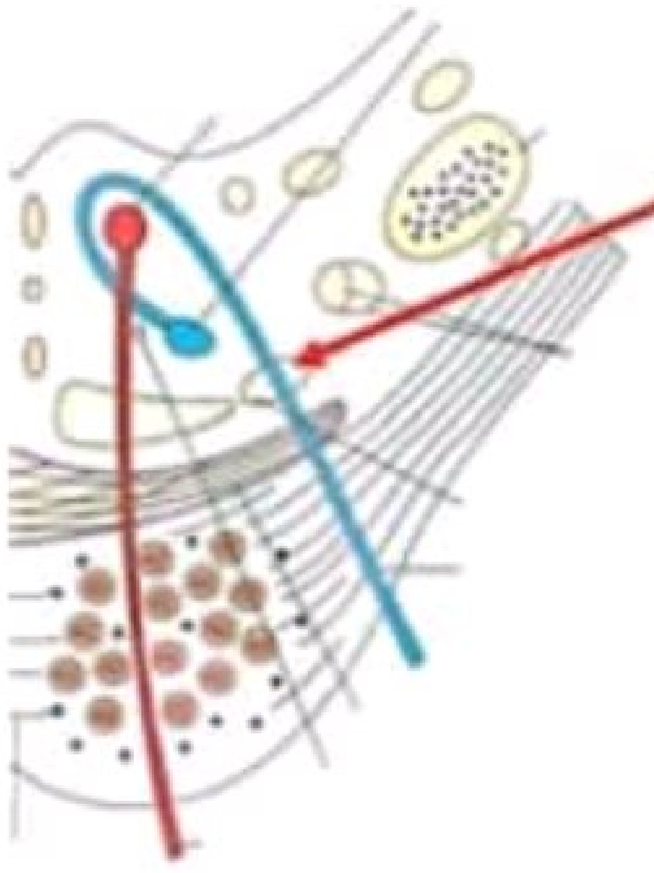

Corticospinal tract

Contralateral hemiplegia

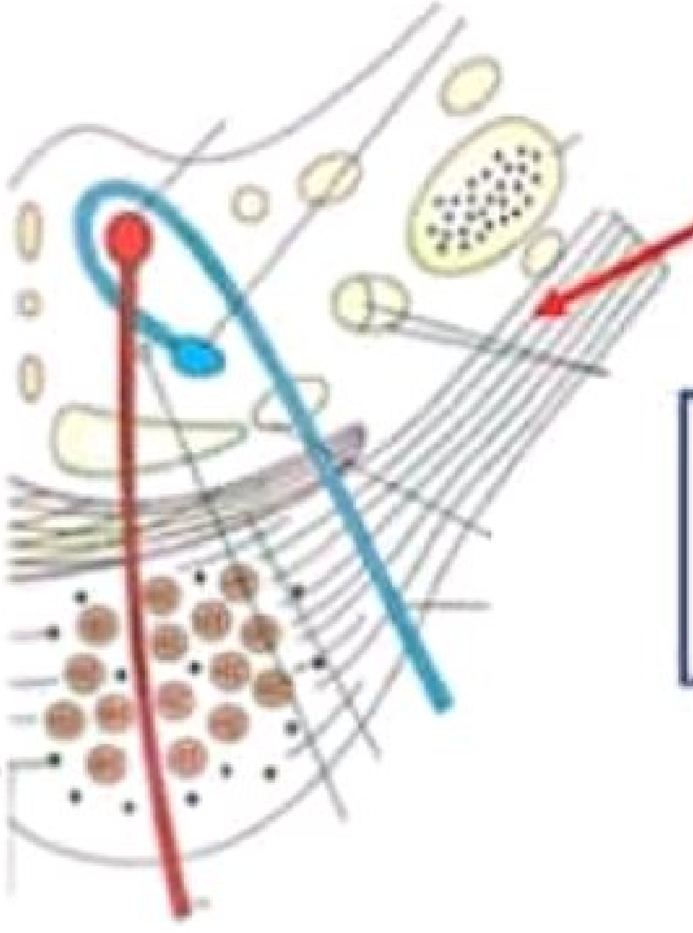

medial lemniscus

Contralateral loss of position and vibration sense

LATERAL PONTINE SYNDROME = MARIE FOX SYNDROME

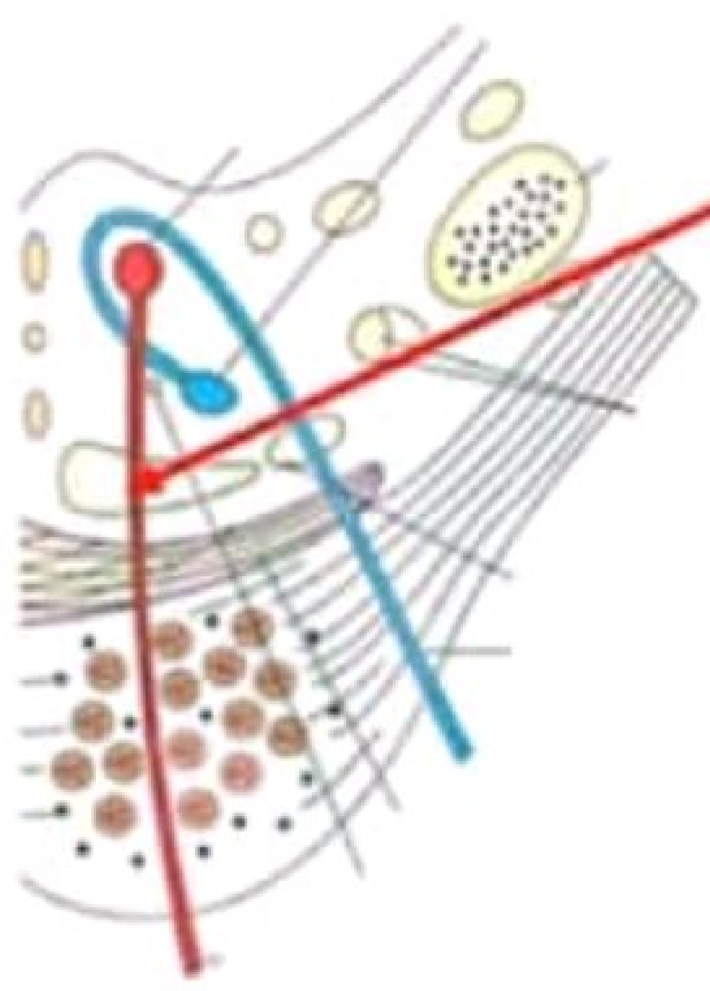

SPINAL LEMNISCUS

CONTRALATERAL LOSS OF PAIN & TEMPERATURE SENSATION OVER THE BODY

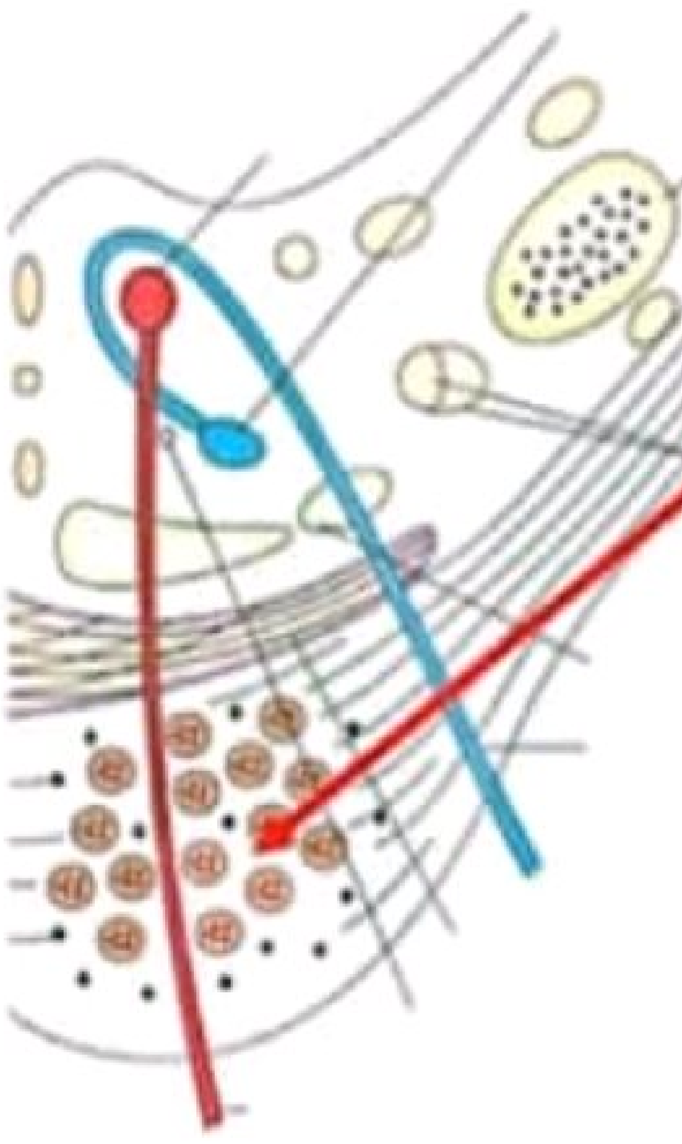

MIDDLE CEREBELLAR PEDUNCLE

ATAXIA

REYMOND CESTON SYNDROME

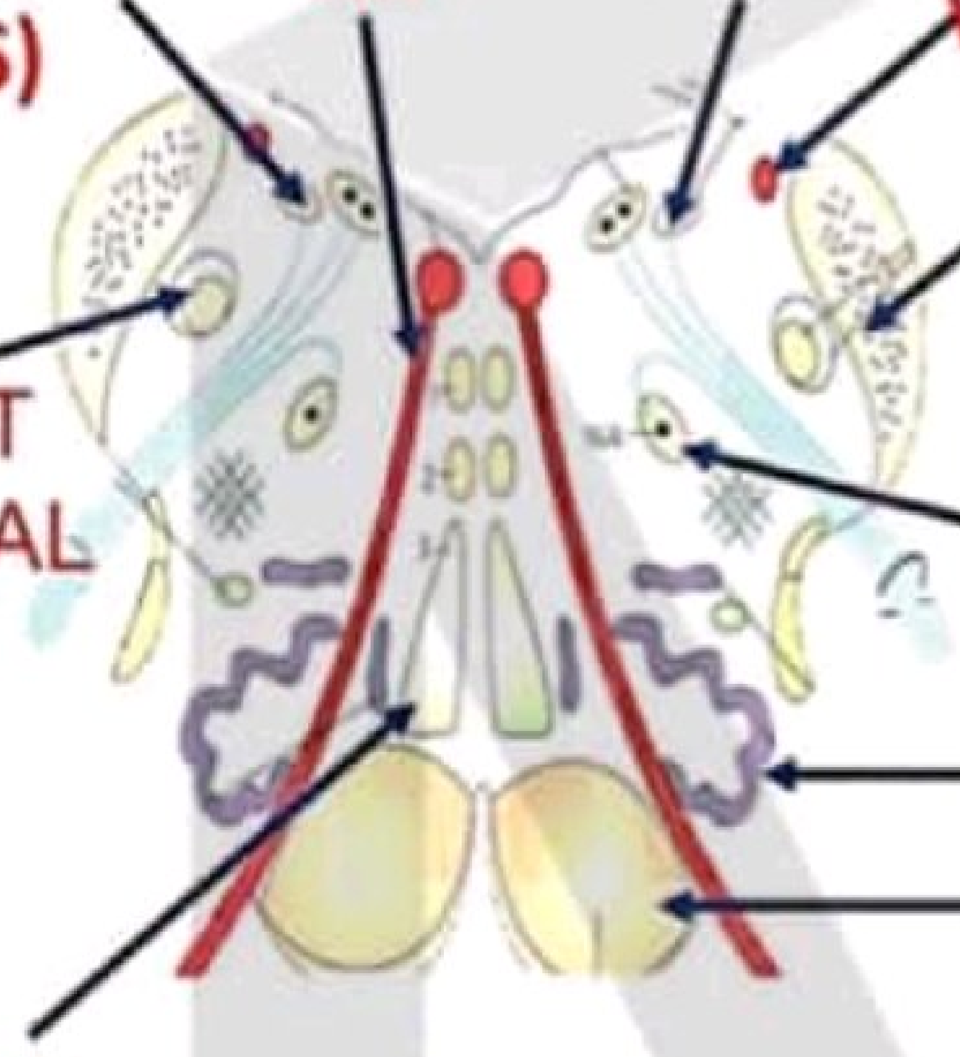


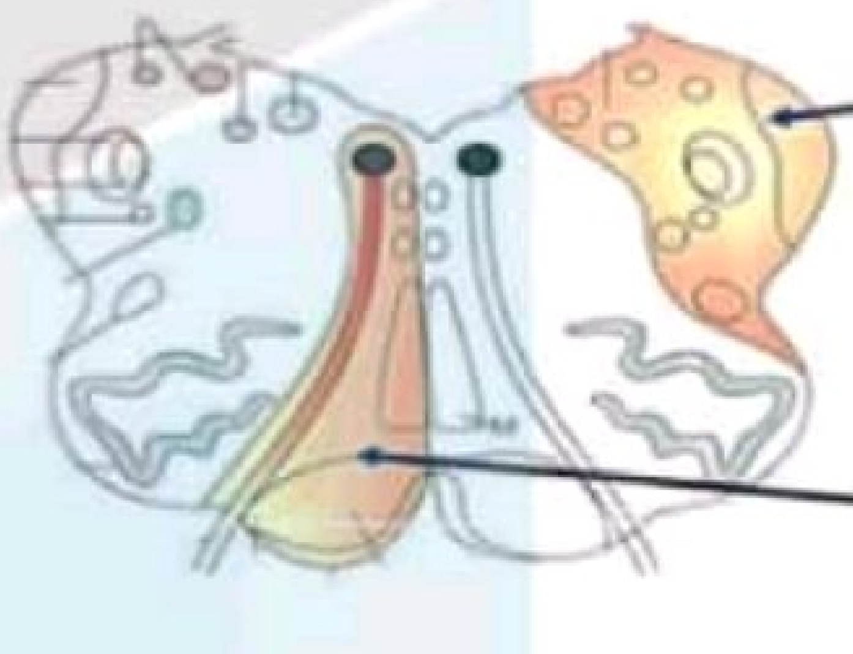
- Medial Squint


Corticospinal tract

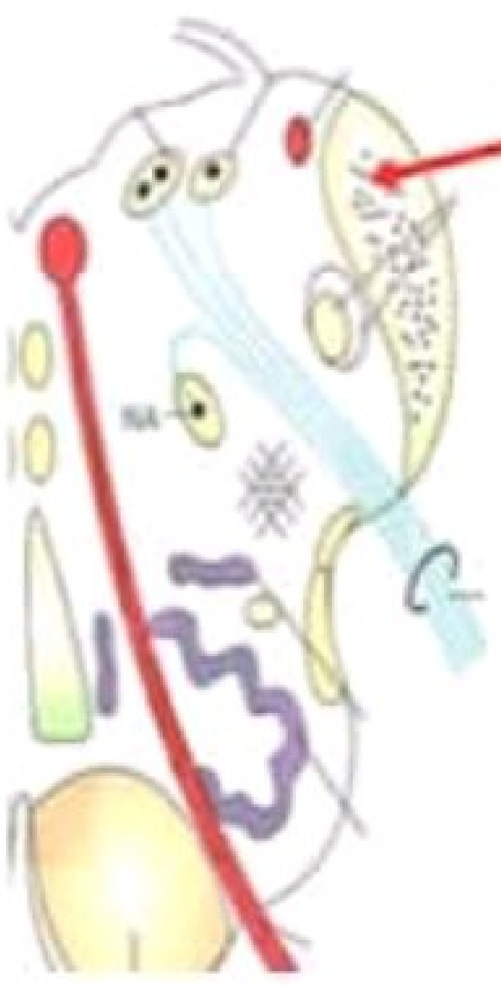
Contralateral hemiplegia

MEDULLA

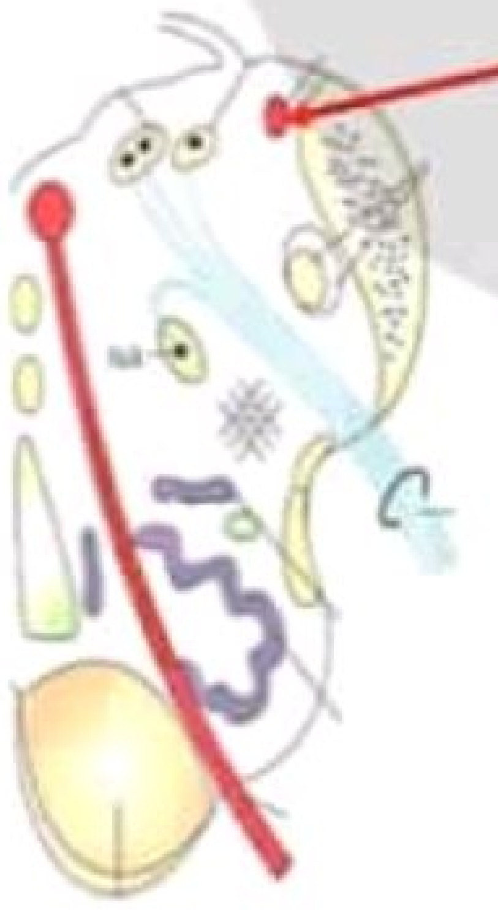

DORSAL N. (VAGUS)
XII
NTS
VESTIBULAR
INF. CEREBELLAR PEDUNCLE
SPINAL TRACT OF TRIGEMINAL NERVE
N. AMBIGUUS
OLIVE
PYRAMID
MEDIAL LEMNISCUS


LATERAL MEDULLARY SYNDROME
MEDIAL MEDULLARY SYNDROME

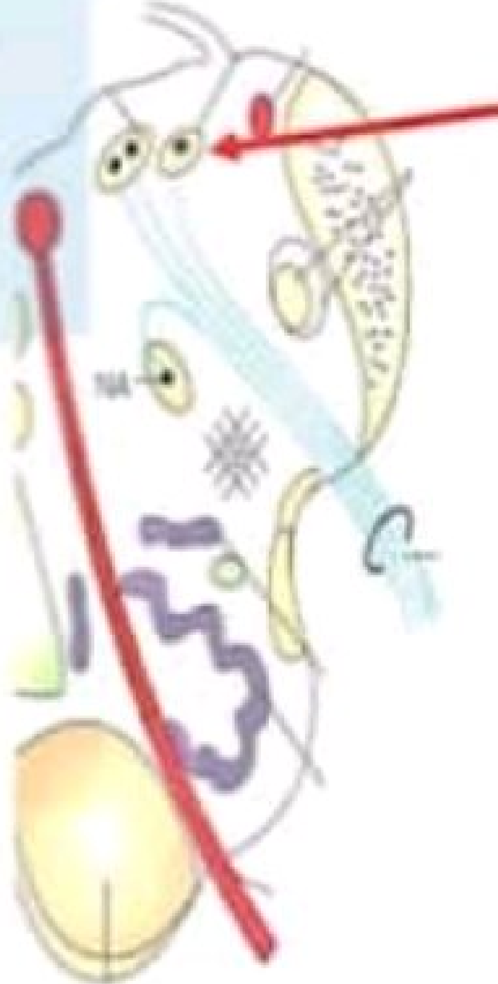
LATERAL MEDULLARY SYNDROME


Inferior cerebellar peduncle

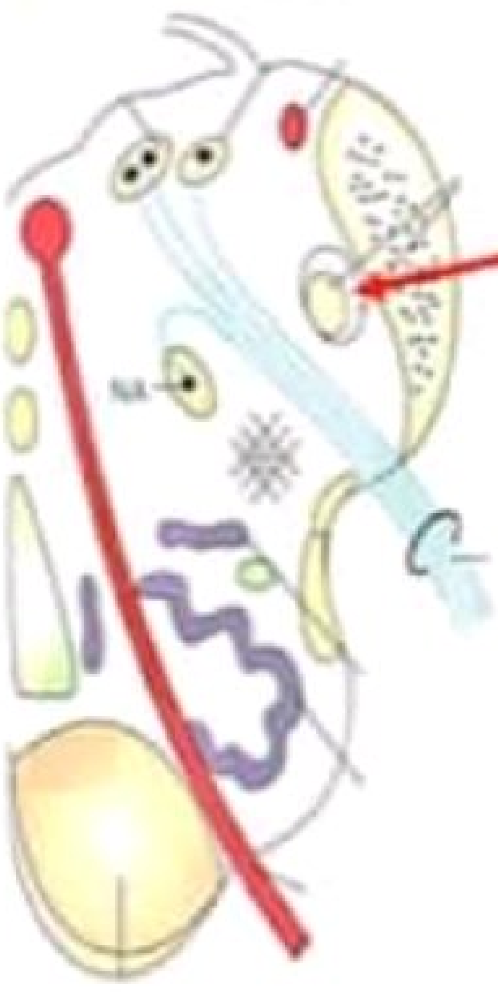
ATAXIA


VESTIBULAR NUCLEUS

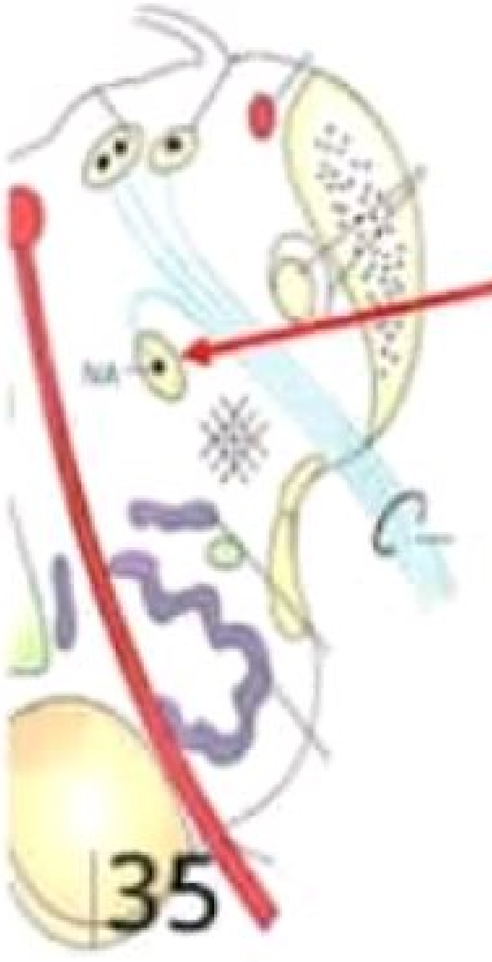
GIDDINESS
NYSTAGMUS
VOMITING



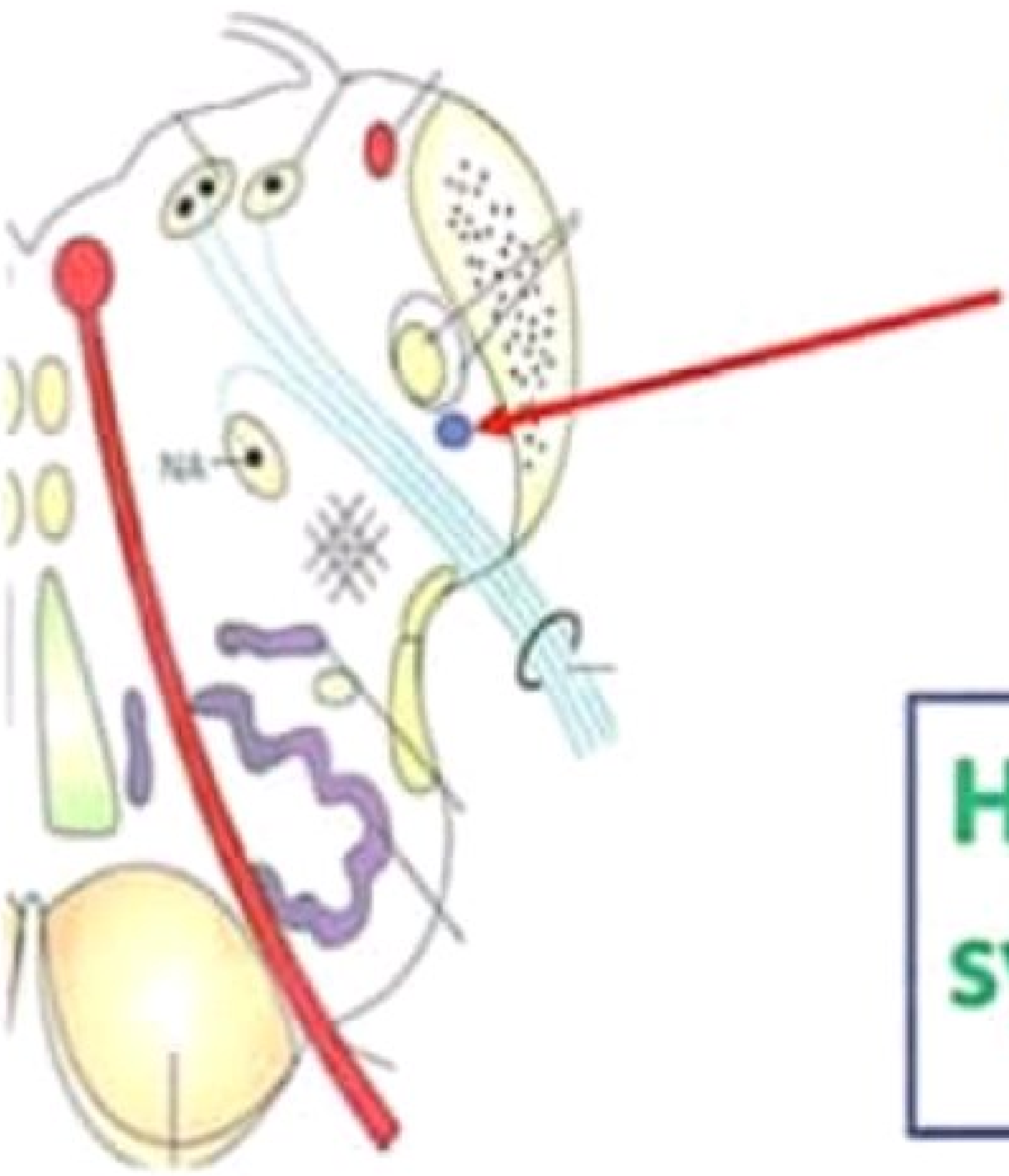
LOSS OF TASTE


SPINAL NUCLEUS AND TRACT OF TRIGEMINAL NERVE

LOSS OF PAIN AND TEMPERATURE SENSATION OVER THE FACE

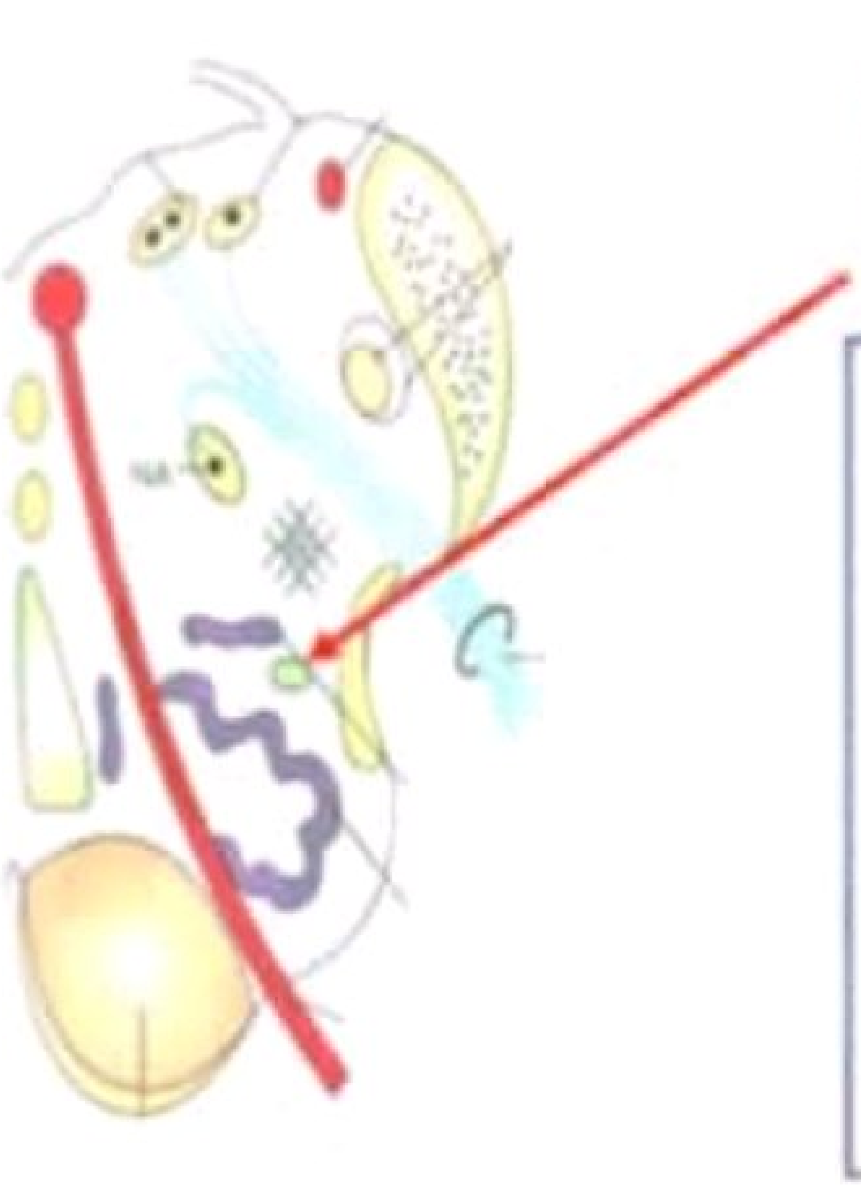

NUCLEUS AMBIGUUS

PARALYSIS OF MUSCLES OF PALATE, PHARYNX & LARYNX



descending sympathetic pathway

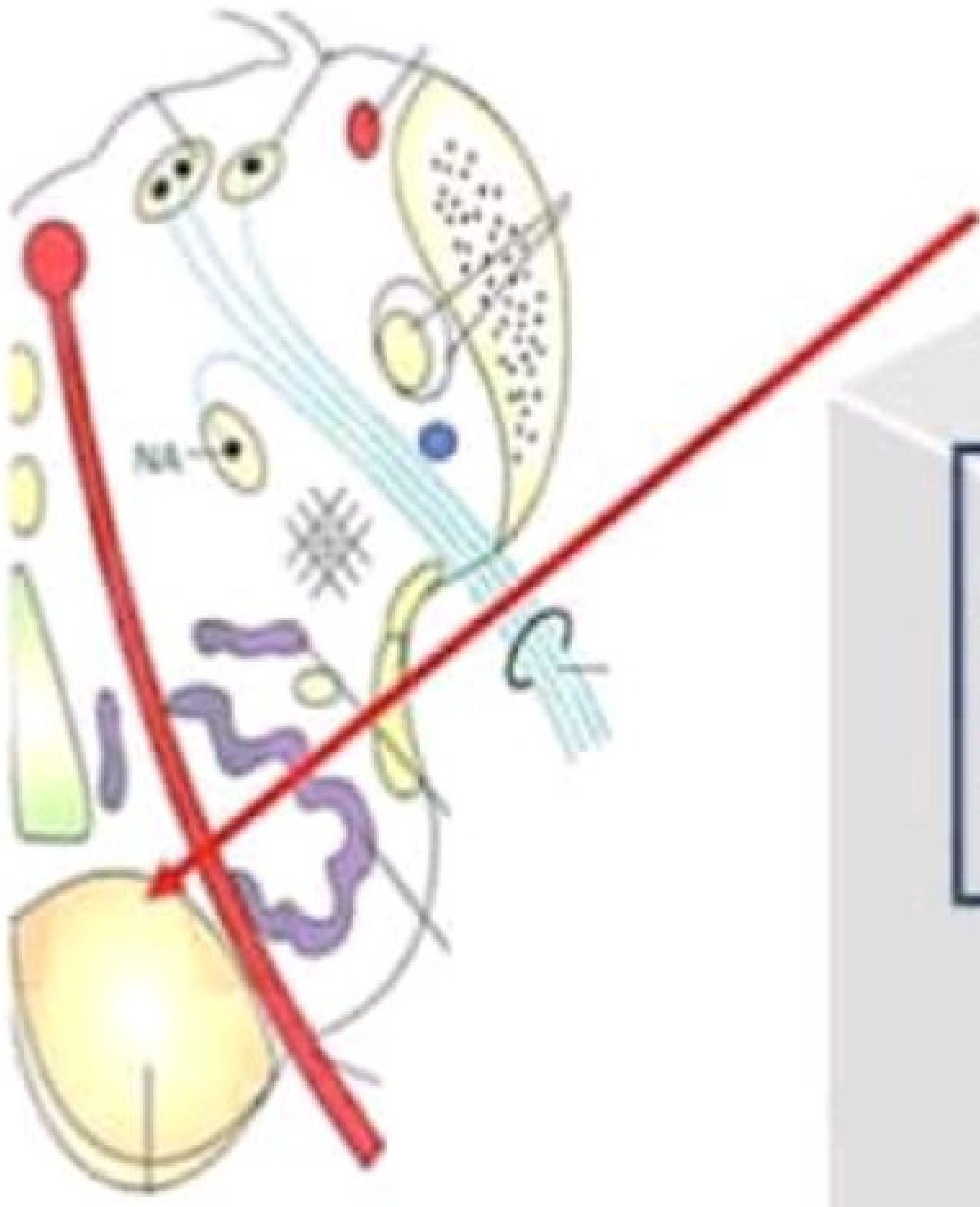
Horner's syndrome



SPINOTHALAMIC TRACT

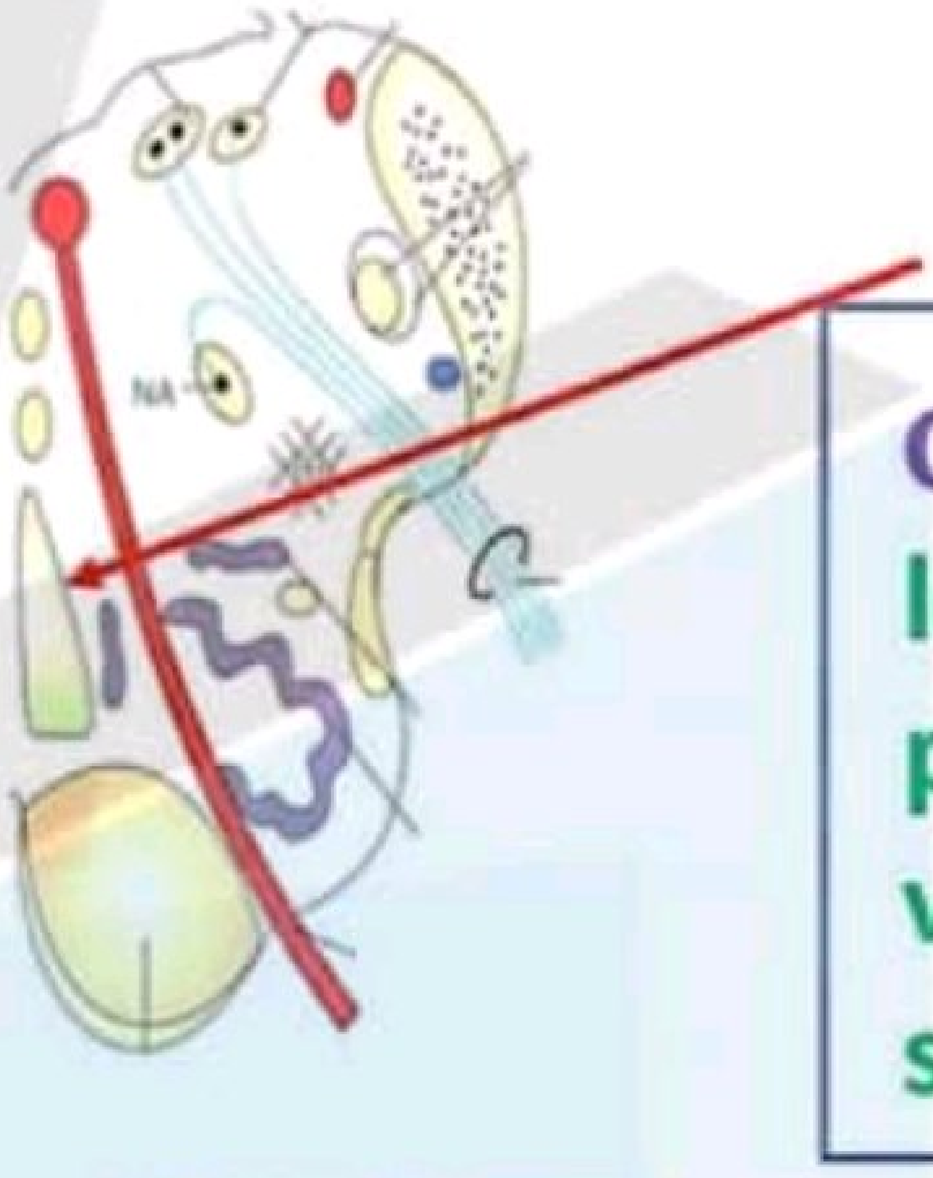
CONTRALATERAL LOSS OF PAIN & TEMPERATURE SENSATION OVER THE BODY

MEDIAL MEDULLARY SYNDROME



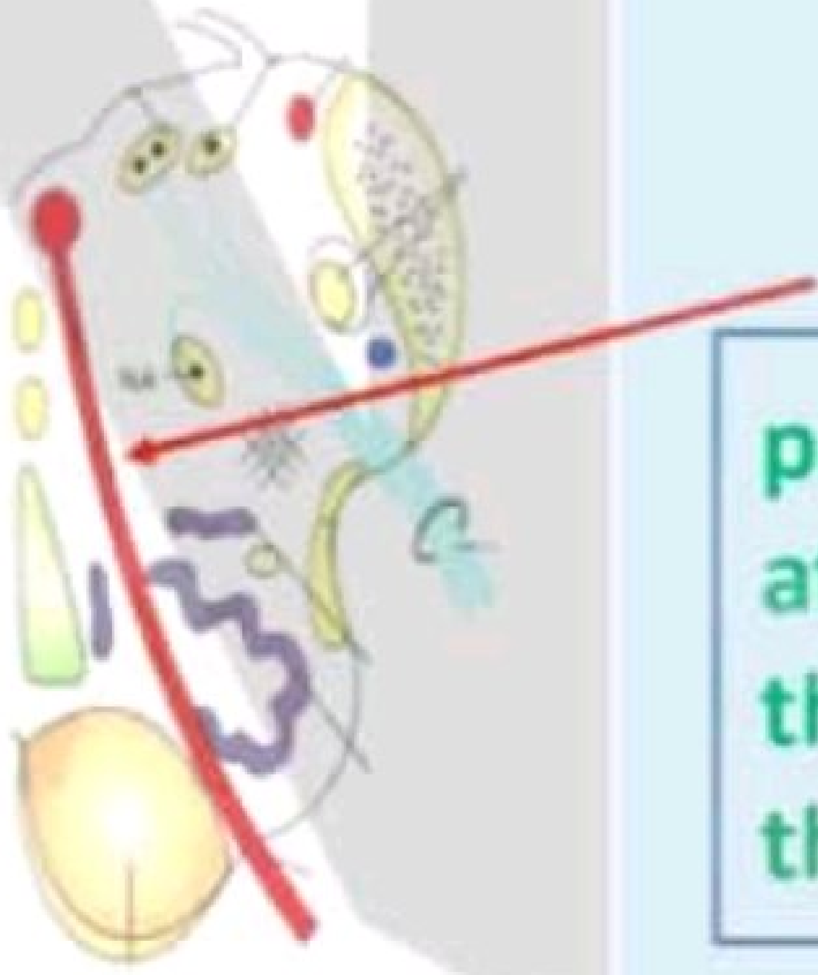
pyramid

Contralateral hemiplegia



medial lemniscus

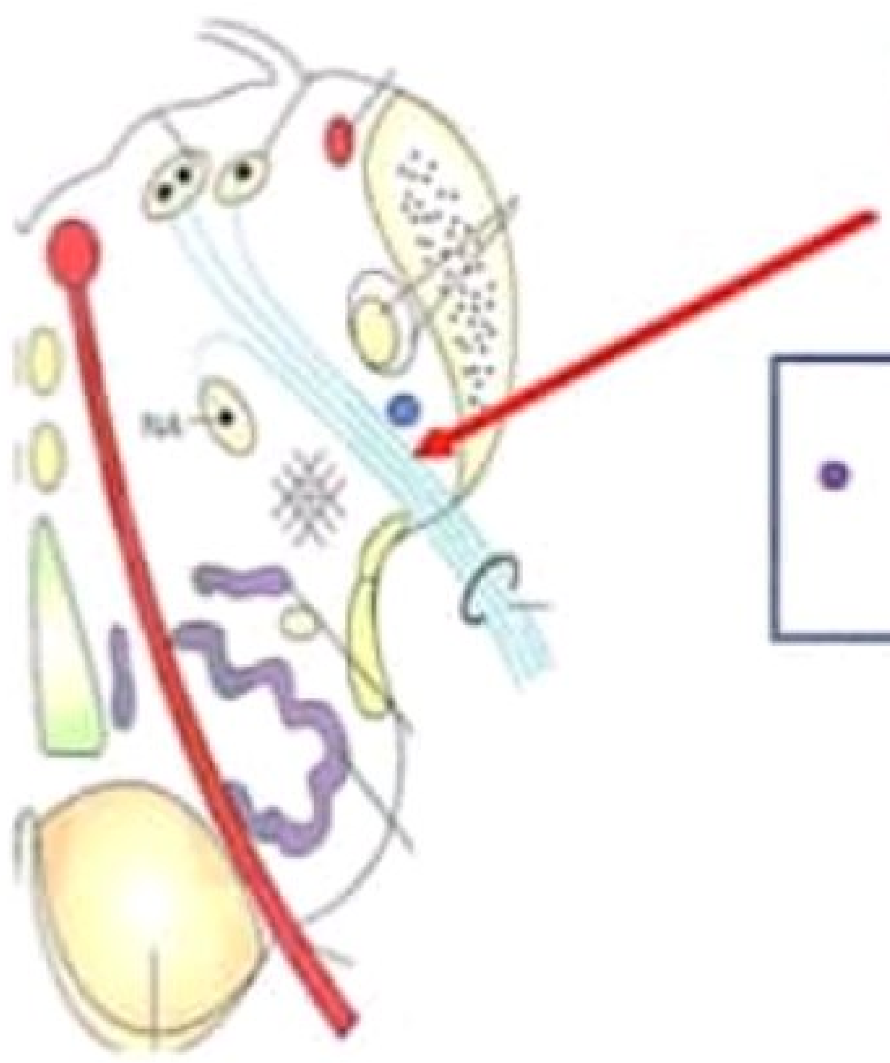
Contralateral loss of position and vibration sense



Hypoglossal nerve

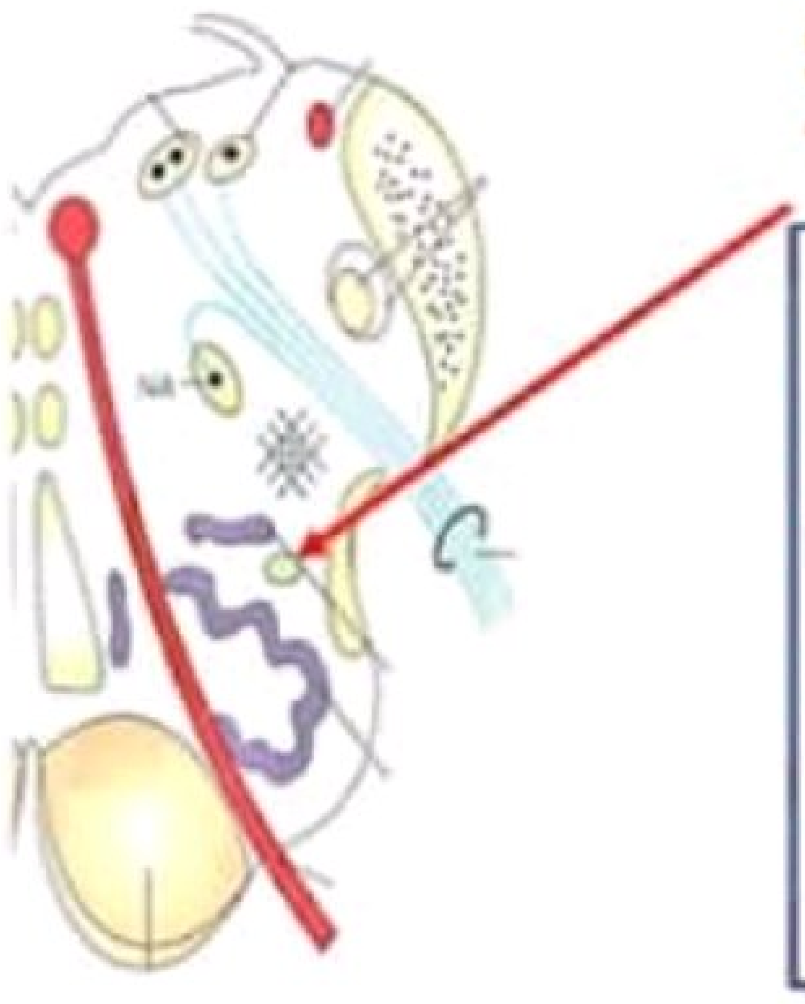
paralysis and atrophy of the half of the tongue

AVILLE'S SYNDROME



VAGUS

- DYSPHAGIA



SPINOTHALAMIC TRACT

CONTRALATERAL LOSS OF PAIN & TEMPERATURE SENSATION OVER THE BODY

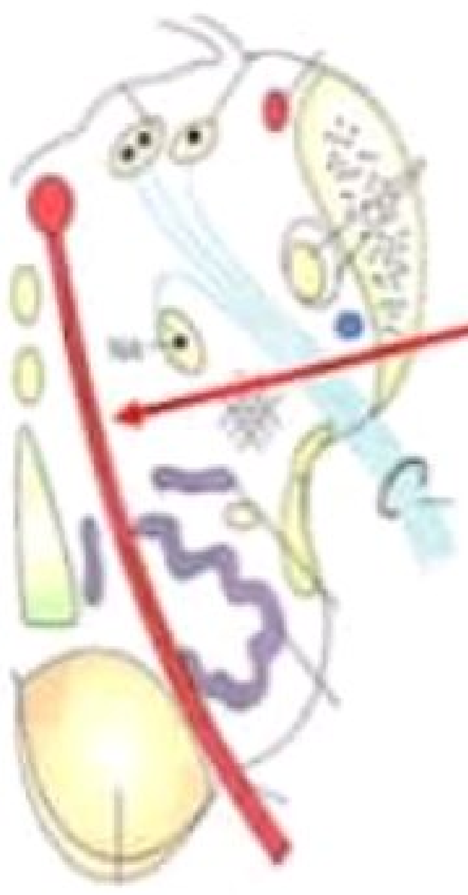
JACKSON SYNDROME

VAGUS

- DYSPHAGIA

SPINOTHALAMIC TRACT

CONTRALATERAL LOSS OF PAIN & TEMPERATURE SENSATION OVER THE BODY



Hypoglossal nerve

paralysis and atrophy of the half of the tongue

DEMENTIA- MAJOR NEUROCOGNITIVE DISORDER

CLINICAL DIAGNOSIS (DSM 5 CRITERIA)

AMNESIA
- New Learning affected
- Remote Memory affected

6 MONTHS DURATION

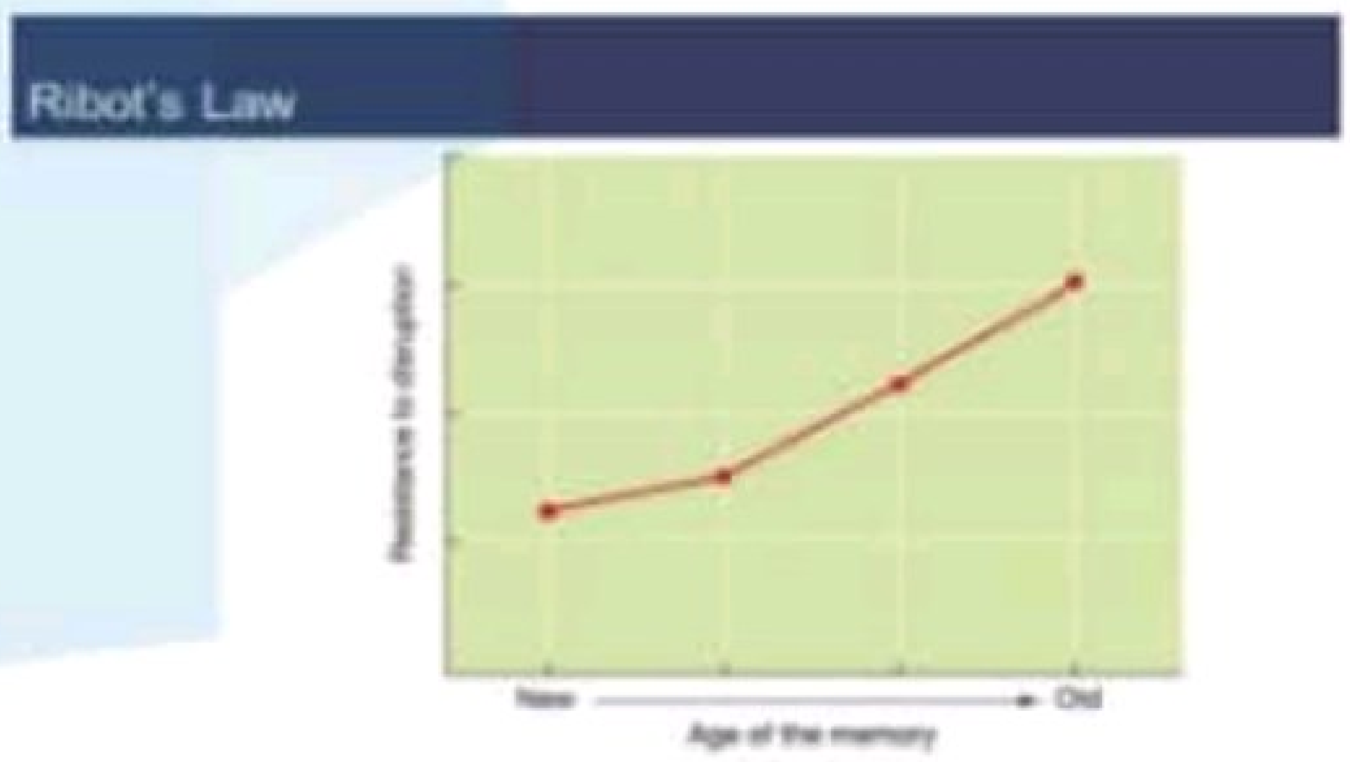
✚ 2 out of 4

1. Apraxia (motor tasks)
2. Agnosia (sensory recognition)
3. Aphasia (speech and language)
4. Loss of executive functions (Planning, organizing, sequencing)

CLEAR SENSORIUM

BEHAVIOURAL SYMPTOMS:

- **Psychosis: in 25% cases**
- **Depression**
- **Personality decline, decreased self-care, lack of drive, apathy**
- **Catastrophic reaction: sudden agitation**



Ribot's Law: Ribot also proposed that old memories are more resistant to disease/disruption than new memories.

OTHER points:

- **PROSPAPAGNOSIA: inability to recognize familiar faces**
- **MMSE is the diagnostic tool for dementia (<24/30)**
- **Only Surgically cause of dementia is : NPH**

Clinical subtyping (suspicion)

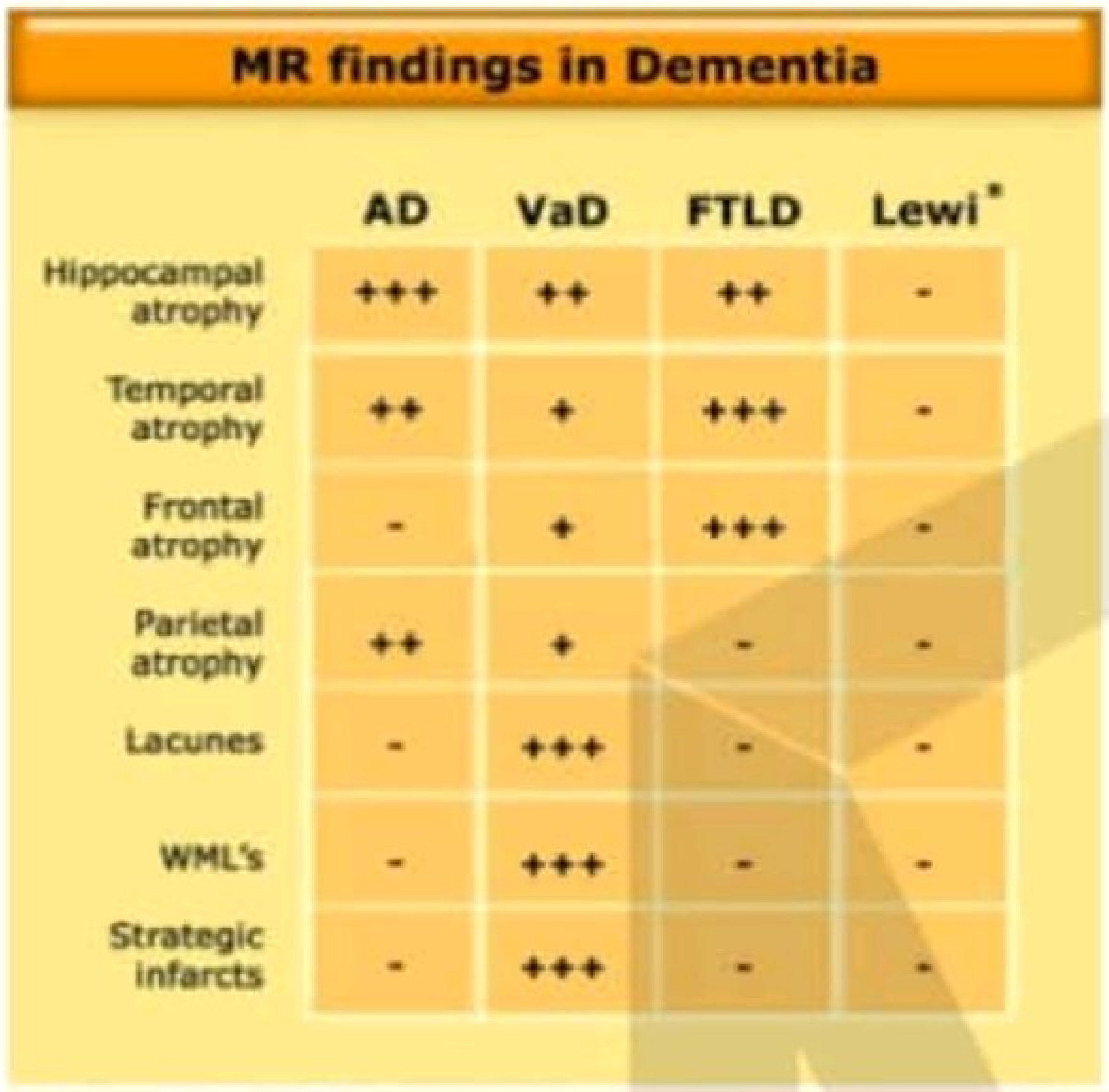
1. Gradually progressive : Alzheimer's (MC)
2. Step ladder progression, emotional lability : Vascular
3. Personality and behavioural changes predominant : FTD
4. Visual halln, movement problems, fluctuating : LBD
5. Dementia, Urinary incontinence, Ataxia : NPH
6. Rapidly progressive dementia + Myoclonus : CJD

Evaluation of a case of dementia

(15% cases are reversible)

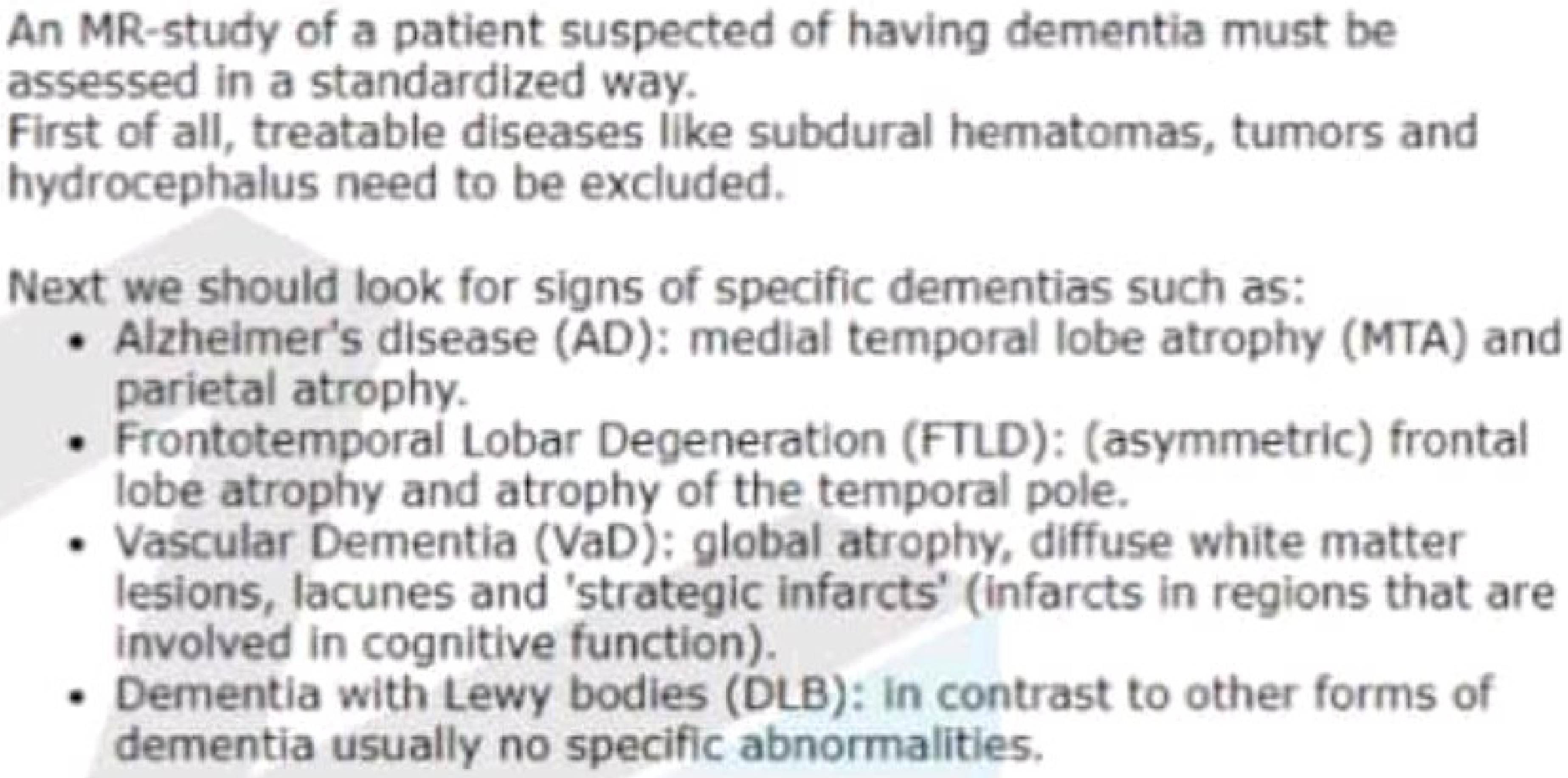
- MRI Brain → NPH
- Thyroid Status → Hypothyroidism
- Vit B12 levels
- Depression: PSUEDODEMENTIA (M/C/C)

RADIOLOGY



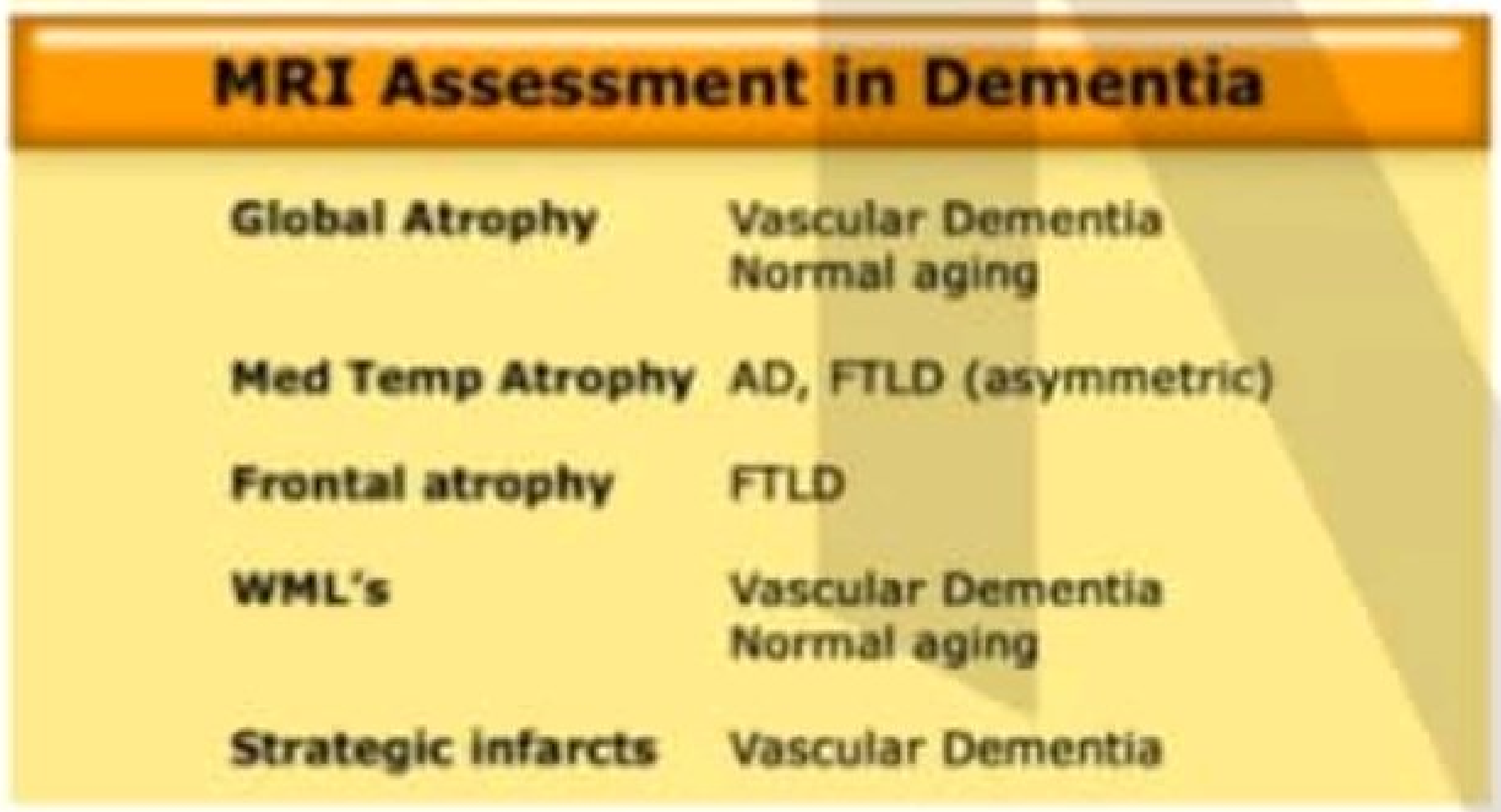
MR findings in Dementia

	AD	VaD	FTLD	Lewi*
Hippocampal atrophy	+++	++	++	-
Temporal atrophy	++	+	+++	-
Frontal atrophy	-	+	+++	-
Parietal atrophy	++	+	-	-
Lacunes	-	+++	-	-
WML's	-	+++	-	-
Strategic infarcts	-	+++	-	-



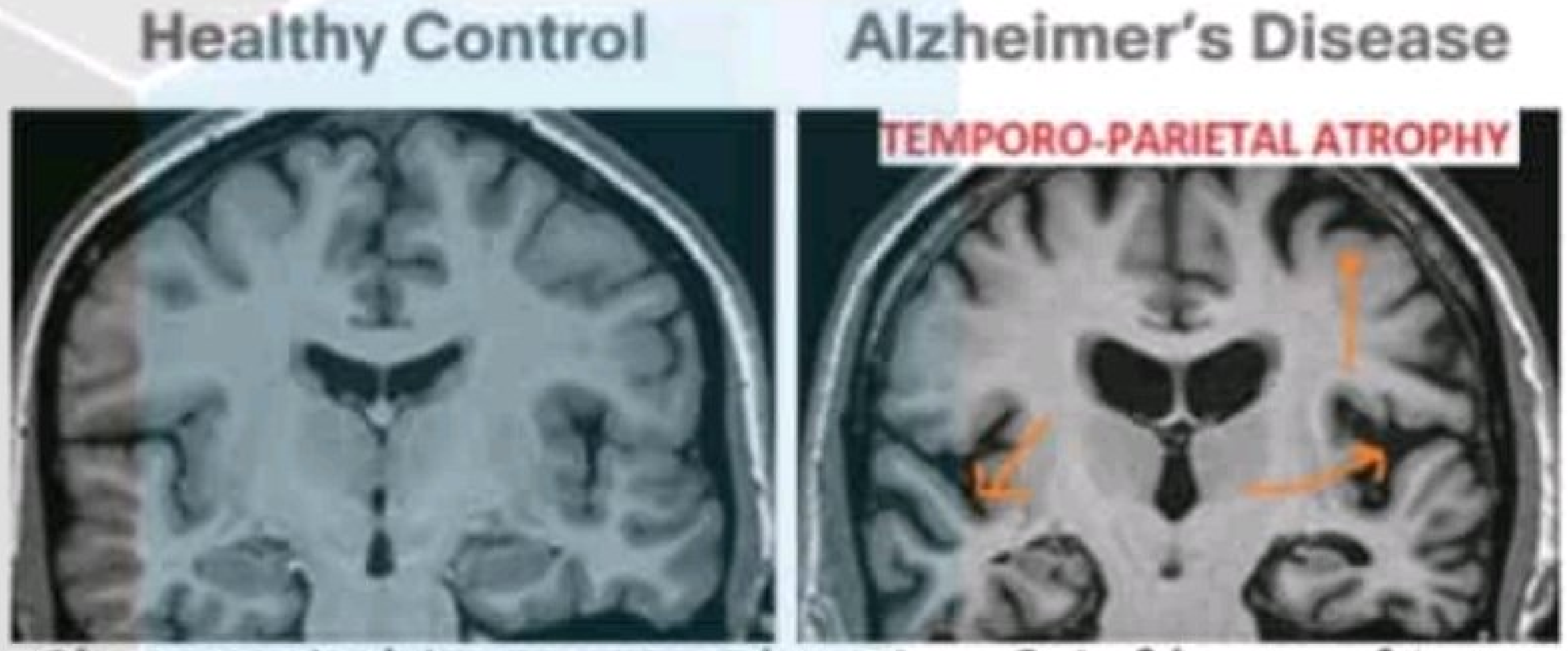
An MR-study of a patient suspected of having dementia must be assessed in a standardized way.
First of all, treatable diseases like subdural hematomas, tumors and hydrocephalus need to be excluded.

Next we should look for signs of specific dementias such as:
- Alzheimer's disease (AD): medial temporal lobe atrophy (MTA) and parietal atrophy.
- Frontotemporal Lobar Degeneration (FTLD): (asymmetric) frontal lobe atrophy and atrophy of the temporal pole.
- Vascular Dementia (VaD): global atrophy, diffuse white matter lesions, lacunes and 'strategic infarcts' (infarcts in regions that are involved in cognitive function).
- Dementia with Lewy bodies (DLB): in contrast to other forms of dementia usually no specific abnormalities.



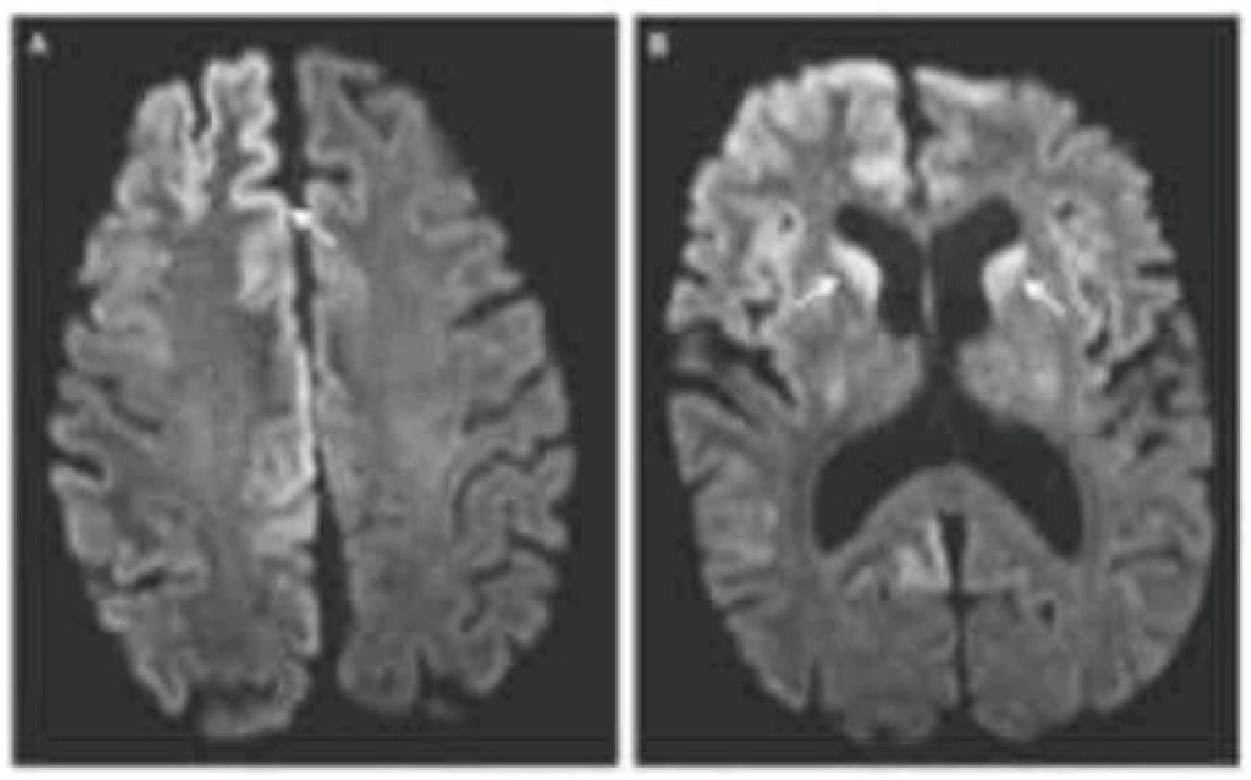
MRI Assessment in Dementia

Global Atrophy	Vascular Dementia Normal aging
Med Temp Atrophy	AD, FTLD (asymmetric)
Frontal atrophy	FTLD
WML's	Vascular Dementia Normal aging
Strategic infarcts	Vascular Dementia



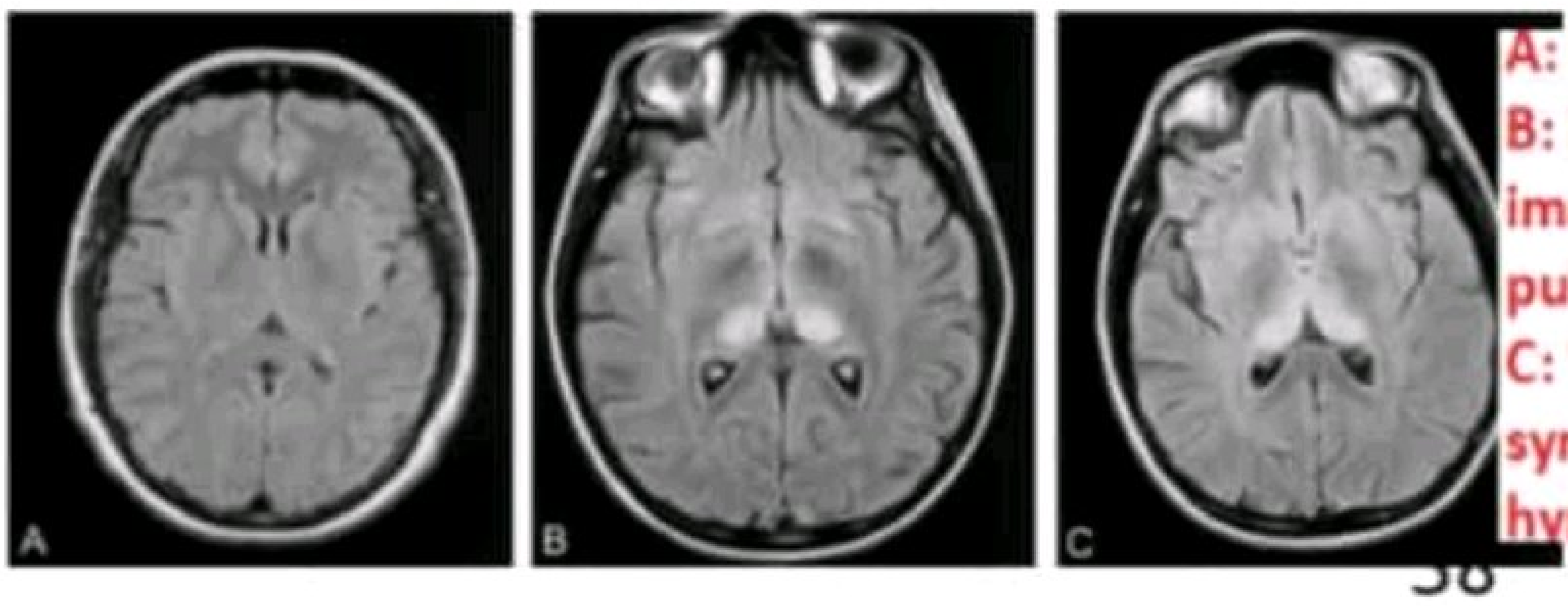
Changes in hippocampal region & inf horn of Lat vent

Creutzfeldt–Jakob disease

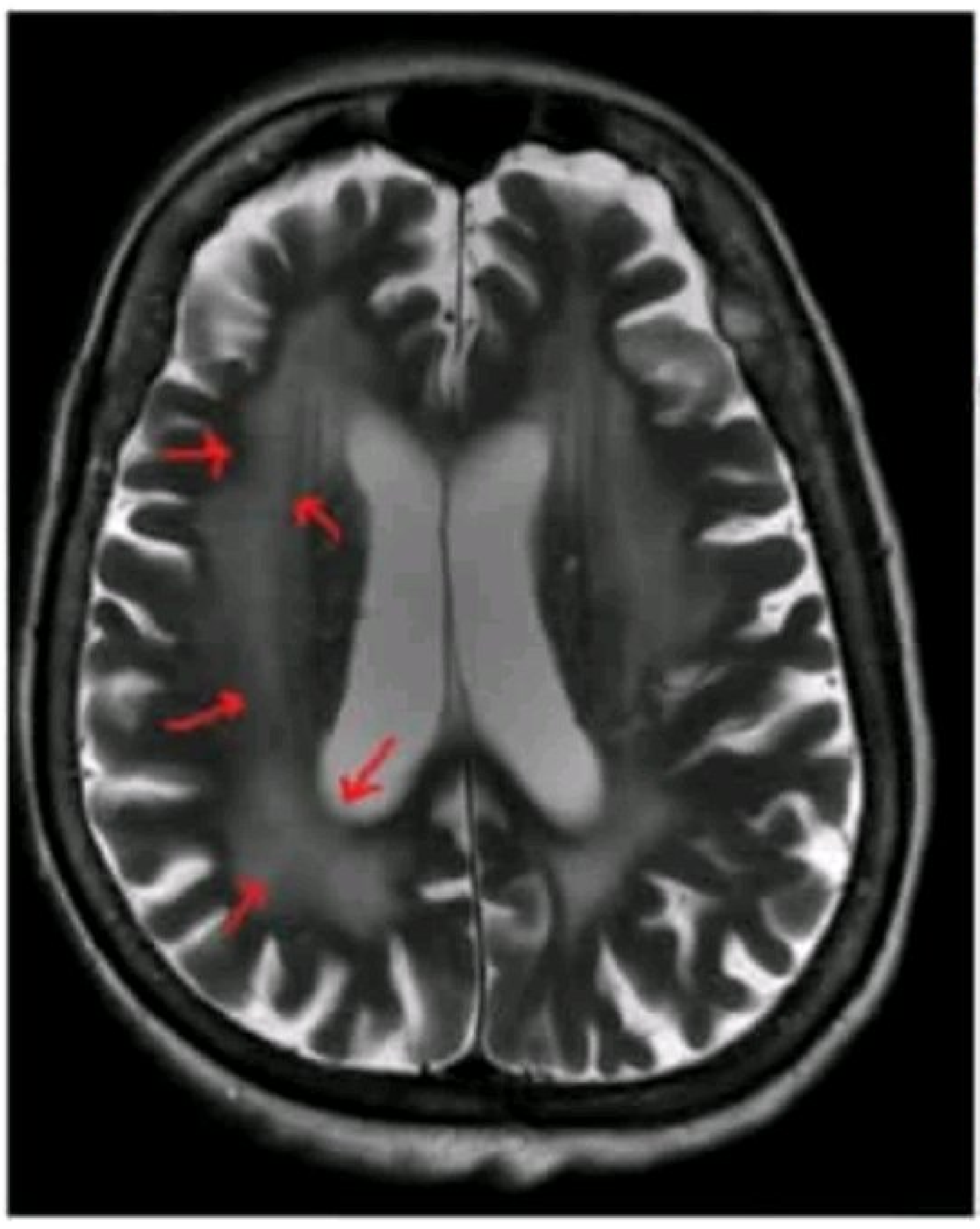


A: Cortical Ribboning (d/t spongiform degeneration)

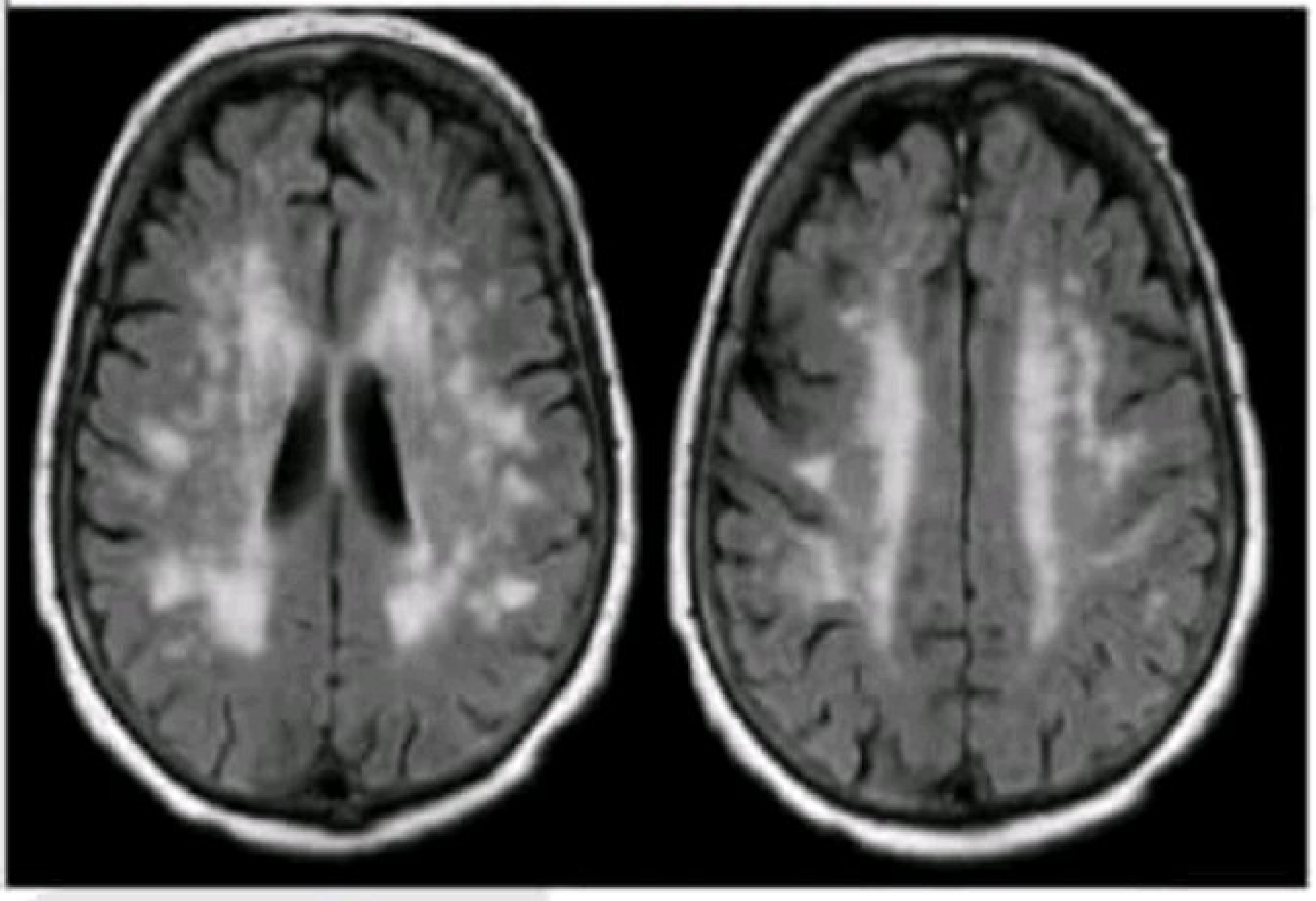
B: Increased signals in the STRIATUM

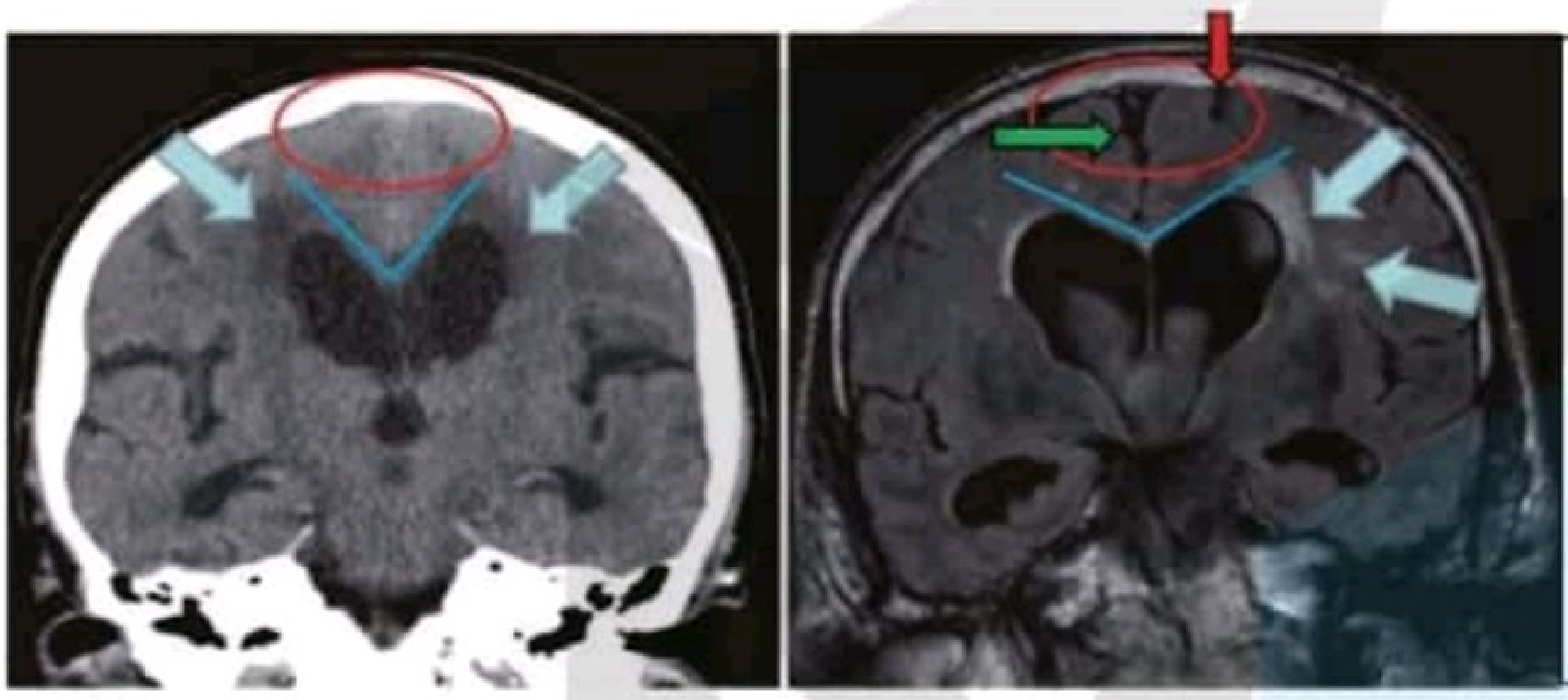


A: Normal
B: Pulvinar sign of variant CJD (MADCOW Disease). FLAIR image shows marked, symmetrical hyperintensity of the pulvinar (posterior) thalamic nuclei.
C: "Hockey-stick" sign of vCJD. FLAIR image shows symmetrical pulvinar and dorsomedial thalamic nuclear hyperintensity.



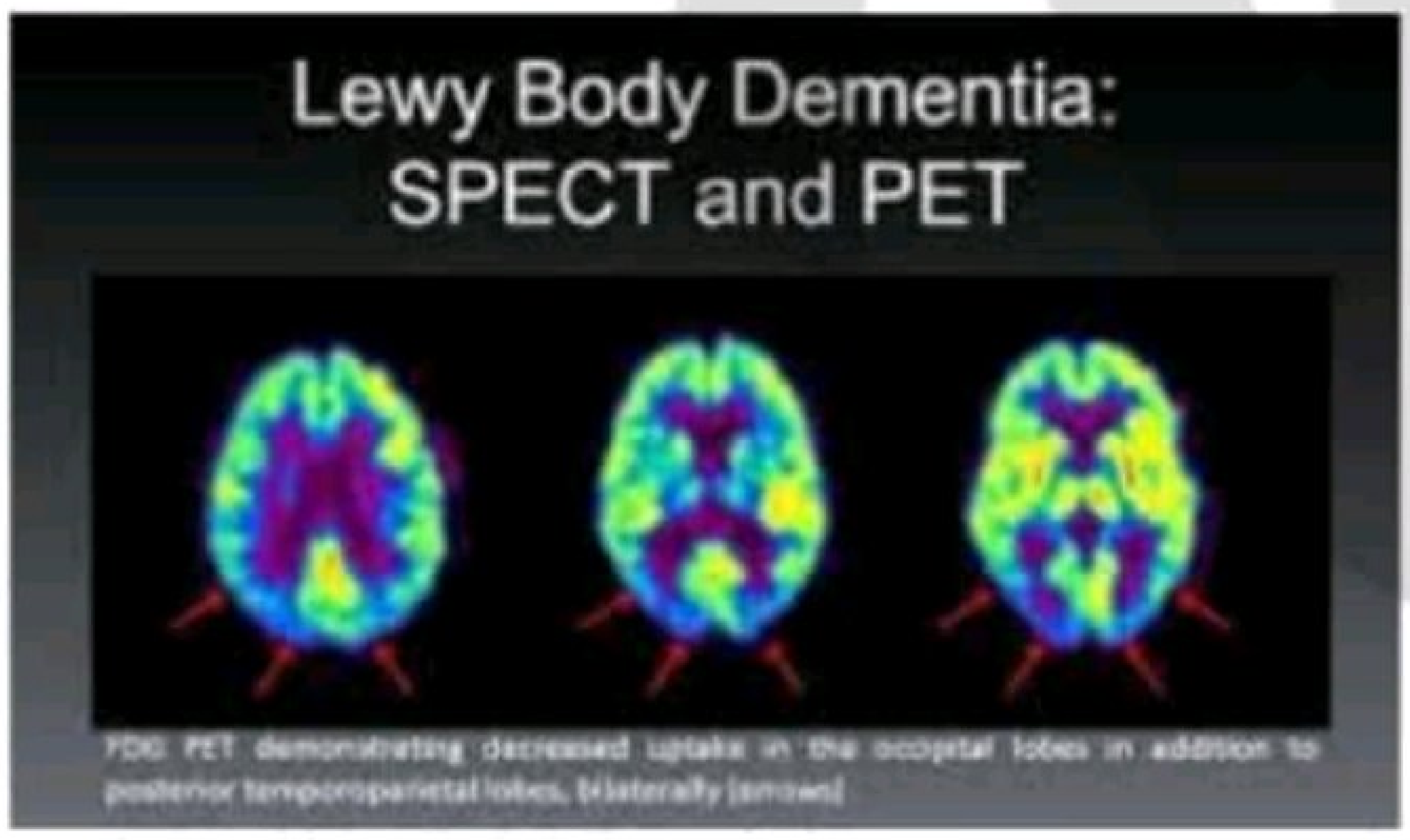
Binswanger's disease, also known as subcortical leukoencephalopathy and subcortical arteriosclerotic encephalopathy (SAE), is a form of small vessel vascular dementia caused by damage to the white brain matter.
Leukoaraiosis is a particular abnormal change in appearance of white matter near the lateral ventricles.





NPH: Normal Pressure Hydrocephalus

- Sulci are not dilated
- Only the ventricle is dilated
- The Callosal Angle (Circle) is ACUTE

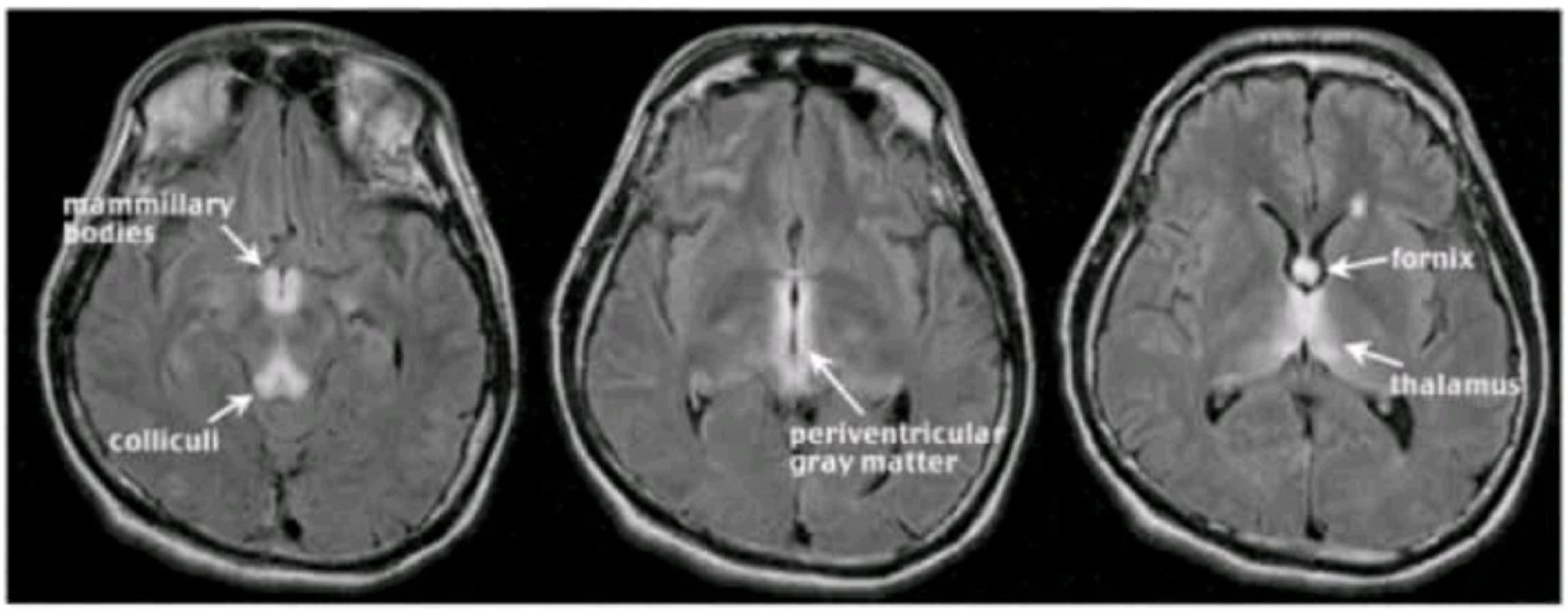


Lewy Body Dementia: SPECT and PET

FDG PET demonstrating decreased uptake in the occipital lobes in addition to posterior temporoparietal lobes, bilaterally (arrows)

Lewy Body Dementia: on SPECT and PET

Reduced FDG Uptake in Occipital Lobe differentiates the LBD from Alzheimer's

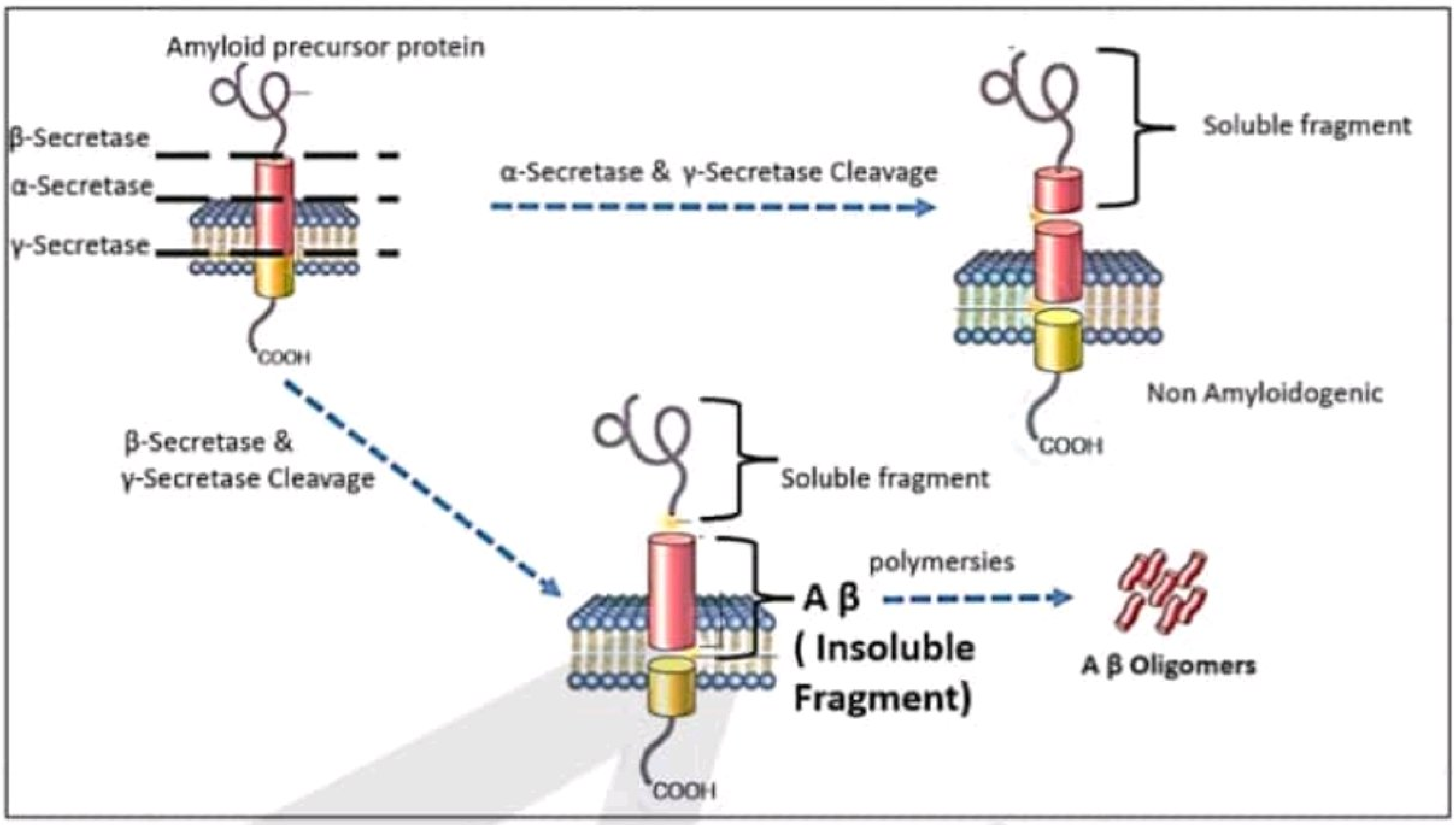


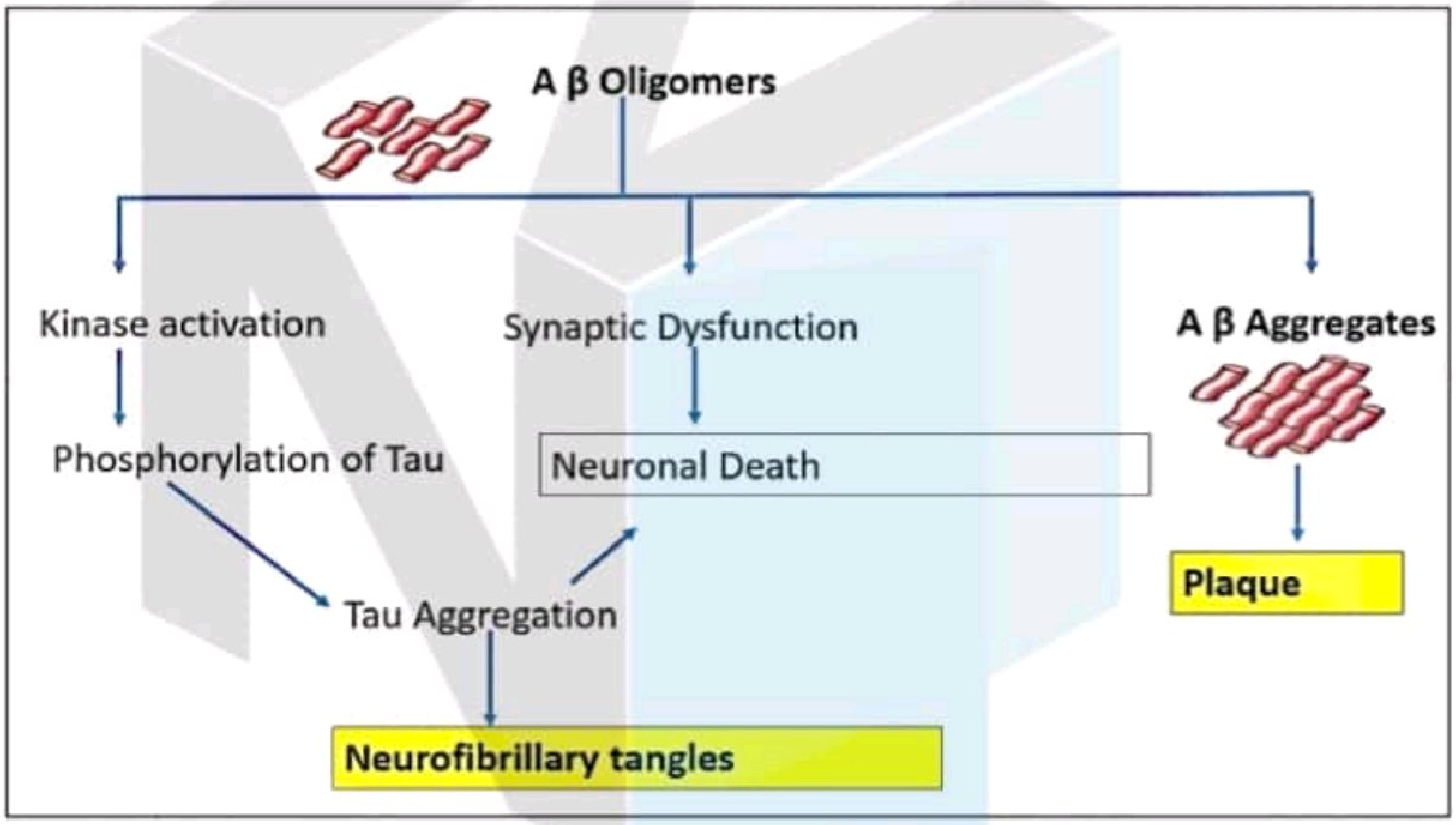
Involvement of different parts in:

Wernicke-Korsakoff Syndrome

(Thiamine deficiency)

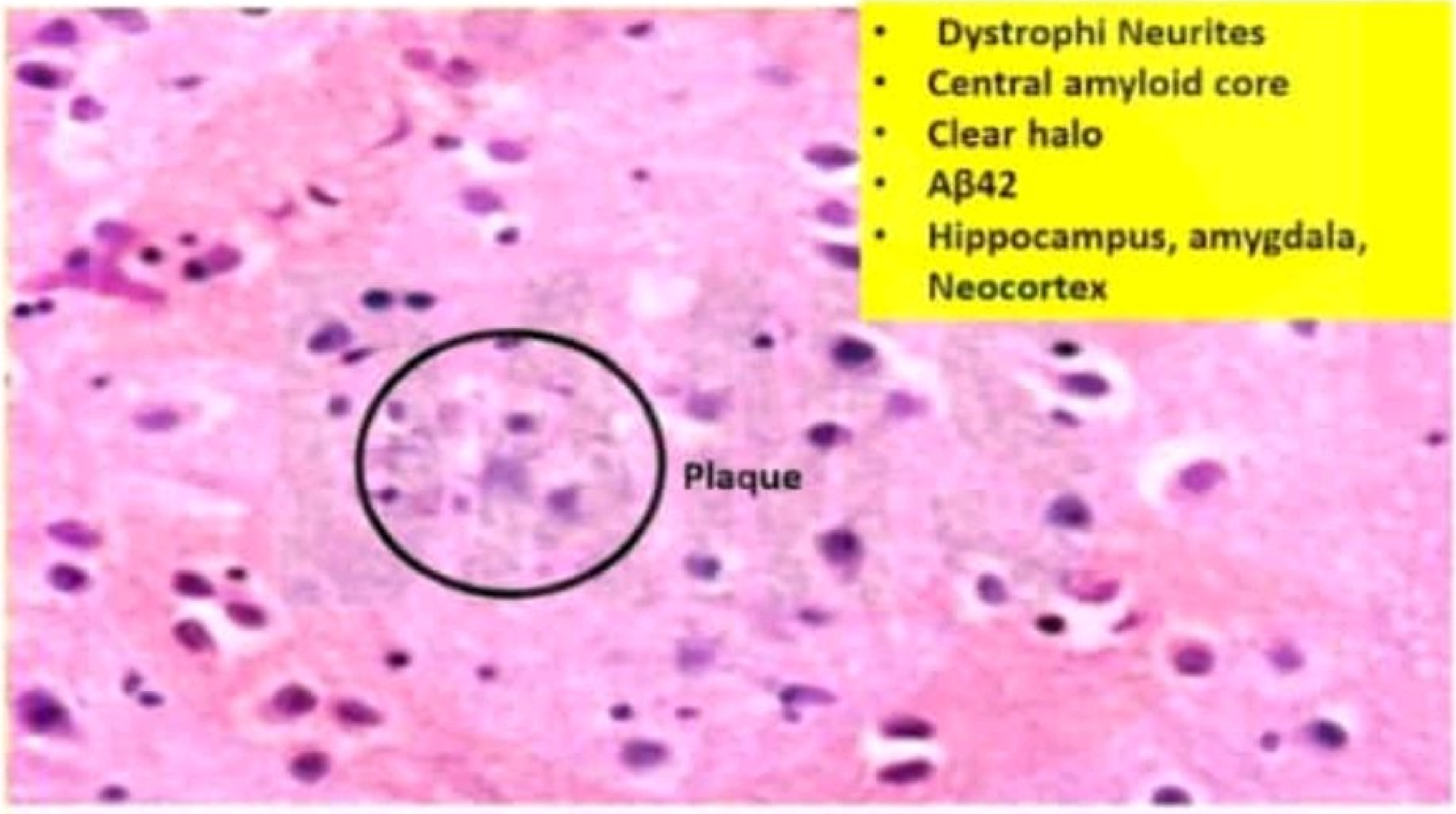
PATHOLOGY


Amyloid precursor protein
β-Secretase
α-Secretase
γ-Secretase
COOH
α-Secretase & γ-Secretase Cleavage
Soluble fragment
Non Amyloidogenic
COOH
β-Secretase &
γ-Secretase Cleavage
Soluble fragment
polymersies
A β
(Insoluble
Fragment)
A β Oligomers
COOH

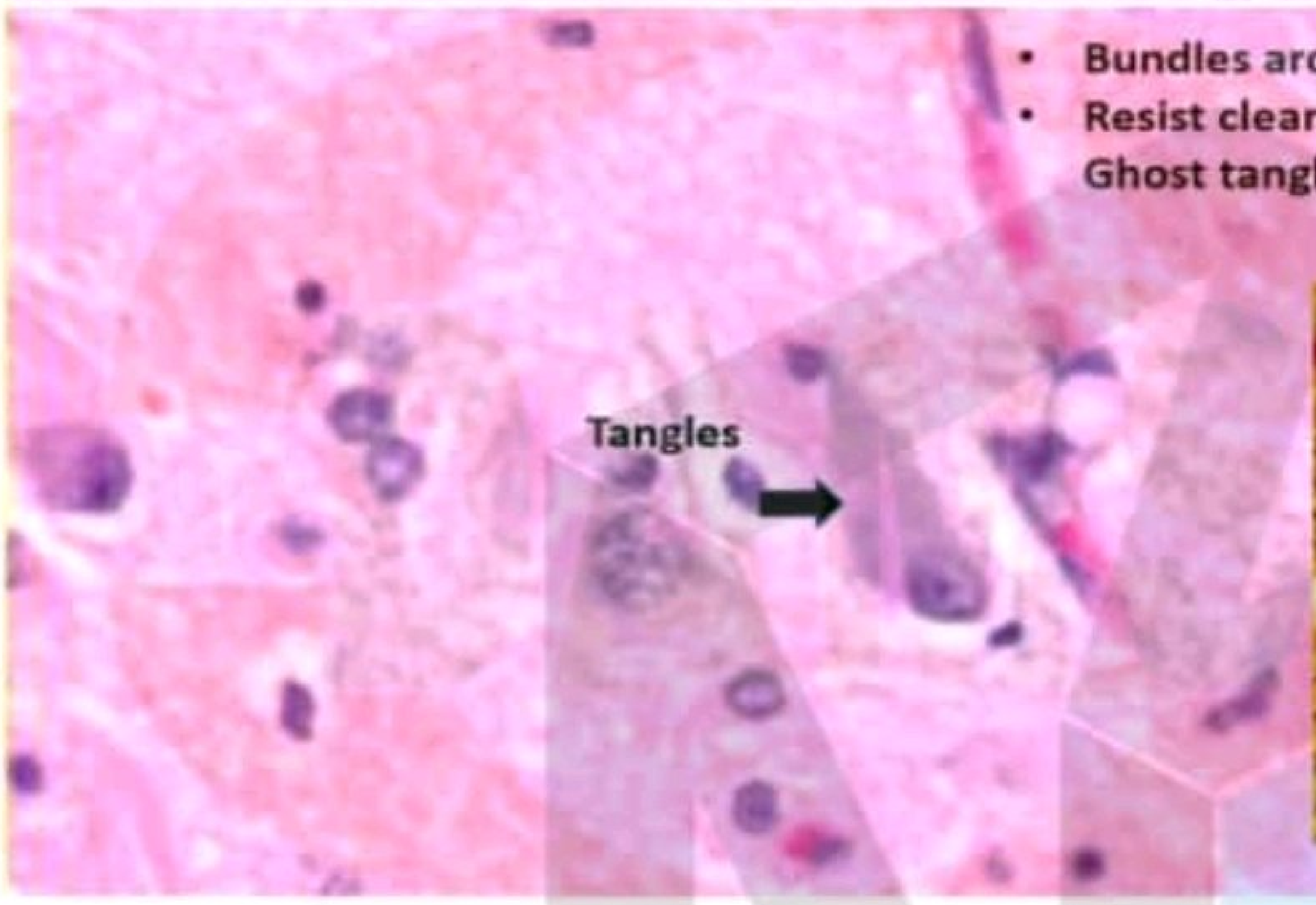

A β Oligomers
Kinase activation
Synaptic Dysfunction
A β Aggregates
Phosphorylation of Tau
Neuronal Death
Plaque
Tau Aggregation
Neurofibrillary tangles

Genetic predisposition

- Presenilin Genes (Majority cause for AD)
  - Presenilin 1 (Chromosome 14), Presenilin 2 (Chromosome 1)
  - Code for gamma secretase
  - Gain of function mutation
- APP gene (Chromosome 21)
  - Downs syndrome extra chromosome more= more APP
- Apolipoprotein E4 (Chromosome 19)
  - Increases Aβ, Tau

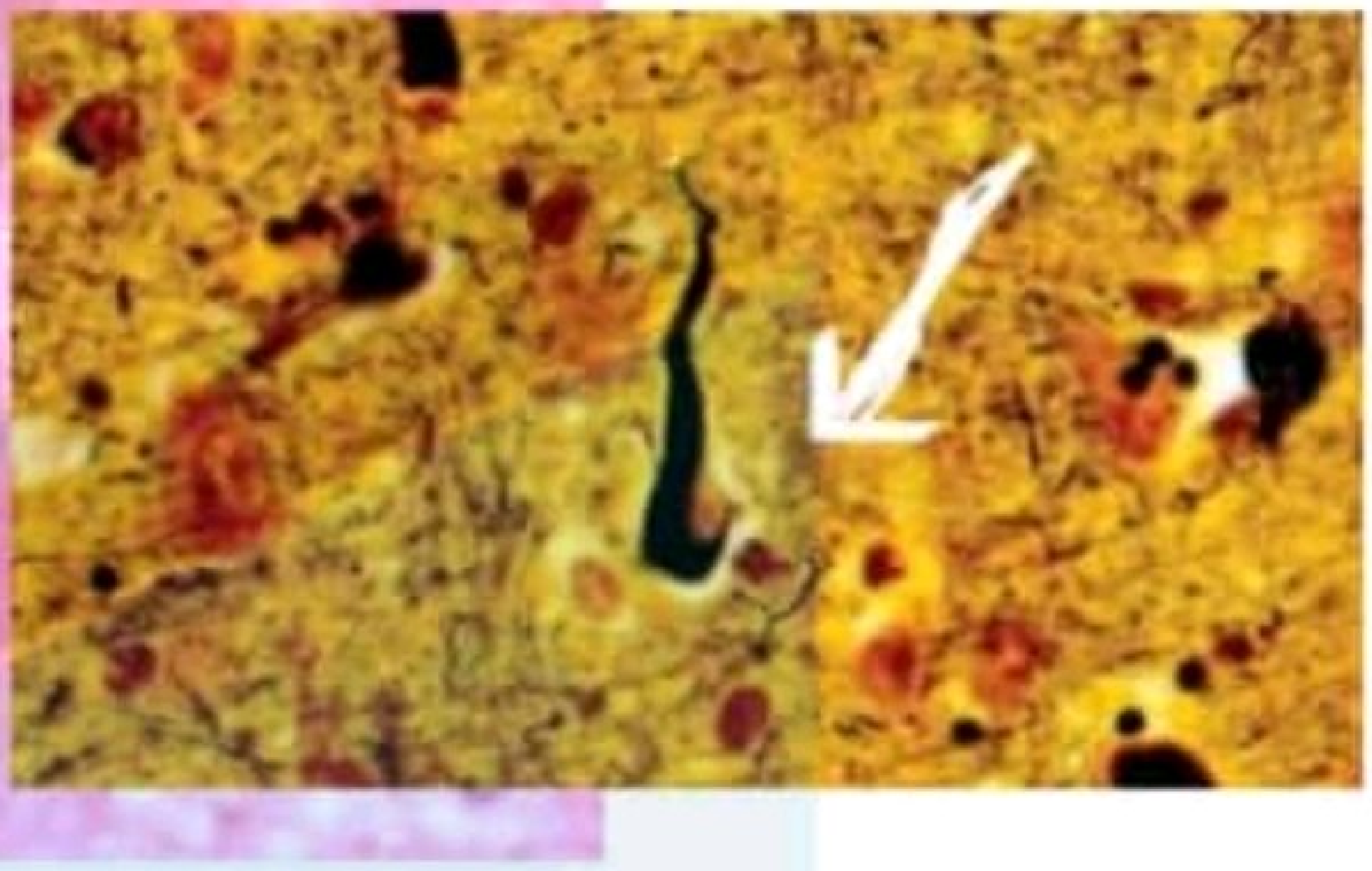


- Dystrophi Neurites
- Central amyloid core
- Clear halo
- Aβ42
- Hippocampus, amygdala, Neocortex

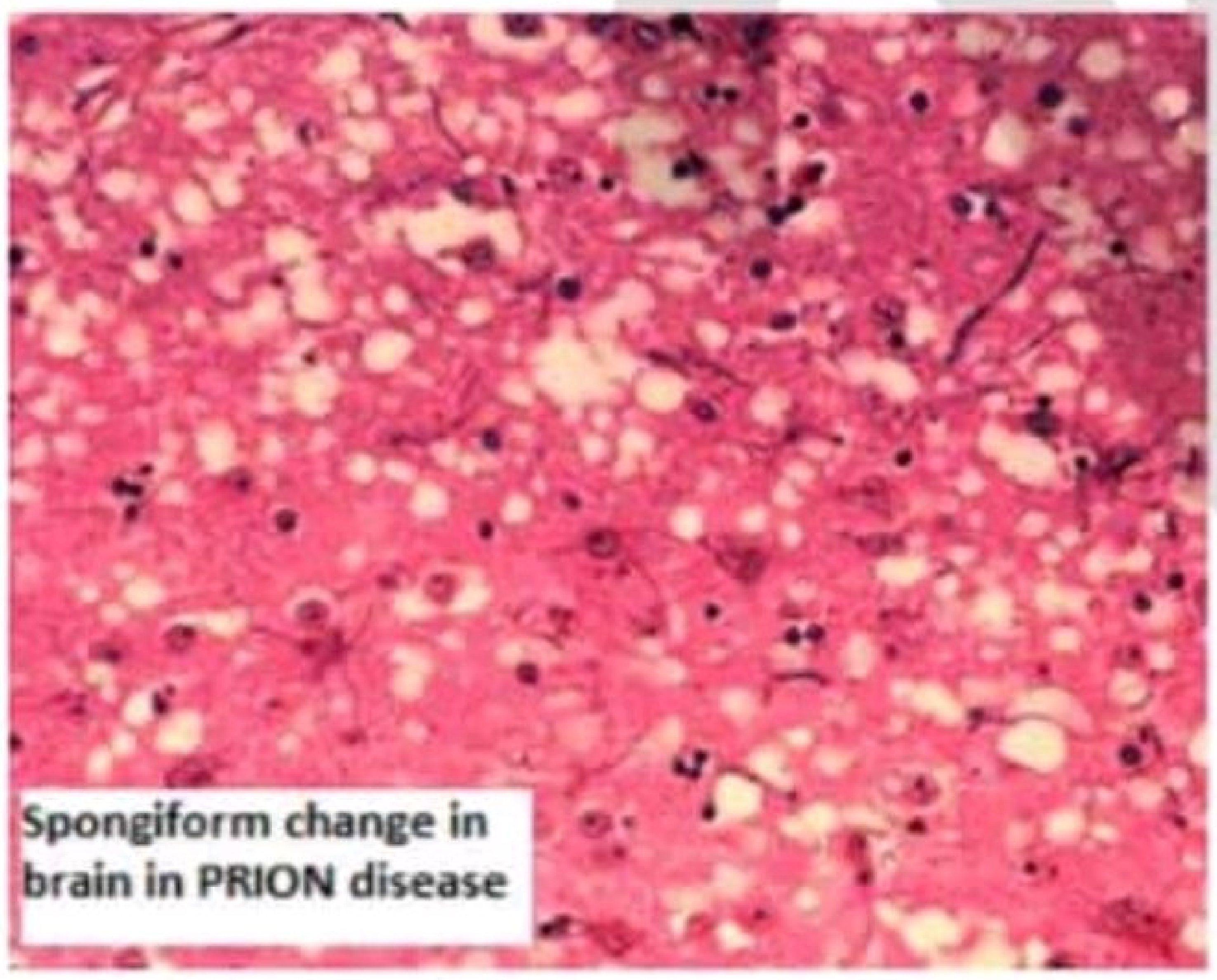


- Bundles around nucleus
- Resist clearance= Tombstone / Ghost tangles

Better Appreciated on Silver Stain



Other CNS diseases:

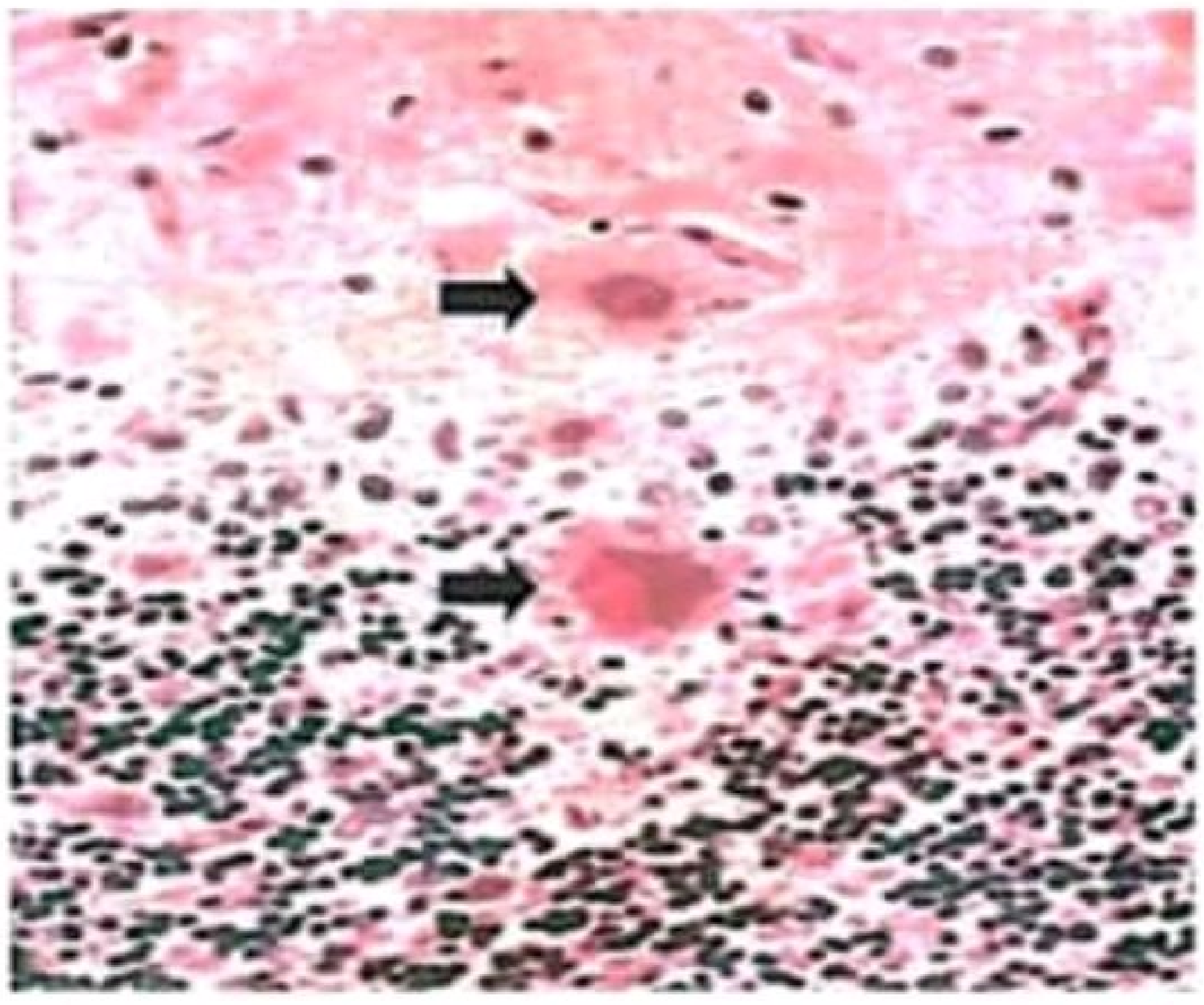


Spongiform change in brain in PRION disease

PRPSC protein deposition in neurons leading to vacuolation of the brain tissue.

(Spongiform Encephalopathies)

Kuru plaque (PRP SC)
Congo red Negative
PAS positive



Disease Group	Protein	Disease
Alzheimer's	Aβ, Tau	Alzheimer's Disease
Tauopathy	Tau	Picks disease, FTD- tau, Progressive Supranuclear Palsy, Global Glial Tauopathy
TDP-43 Prot einopathy	TDP-43	TDP-43, MND
α-Synucleinopathy	α-Synuclein	Parkinson Disease, Lewi Body Dementia, Multiple System Atrophy.
Trinucleotide repeat Disorders	Huntingtin	Huntington's Disease
	Ataxin	Spinocerebellar Ataxia
	FMRP	Fragile X Ataxia Associated Tremor (Repeats 55-200)
	Androgen Receptor	Spinal and bulbar muscular atrophy
Prion Disease	PRP-SC	CJD, FFI, GSS, Kuru Disease

Pharmacology

ALZHEIMER'S DEMENTIA

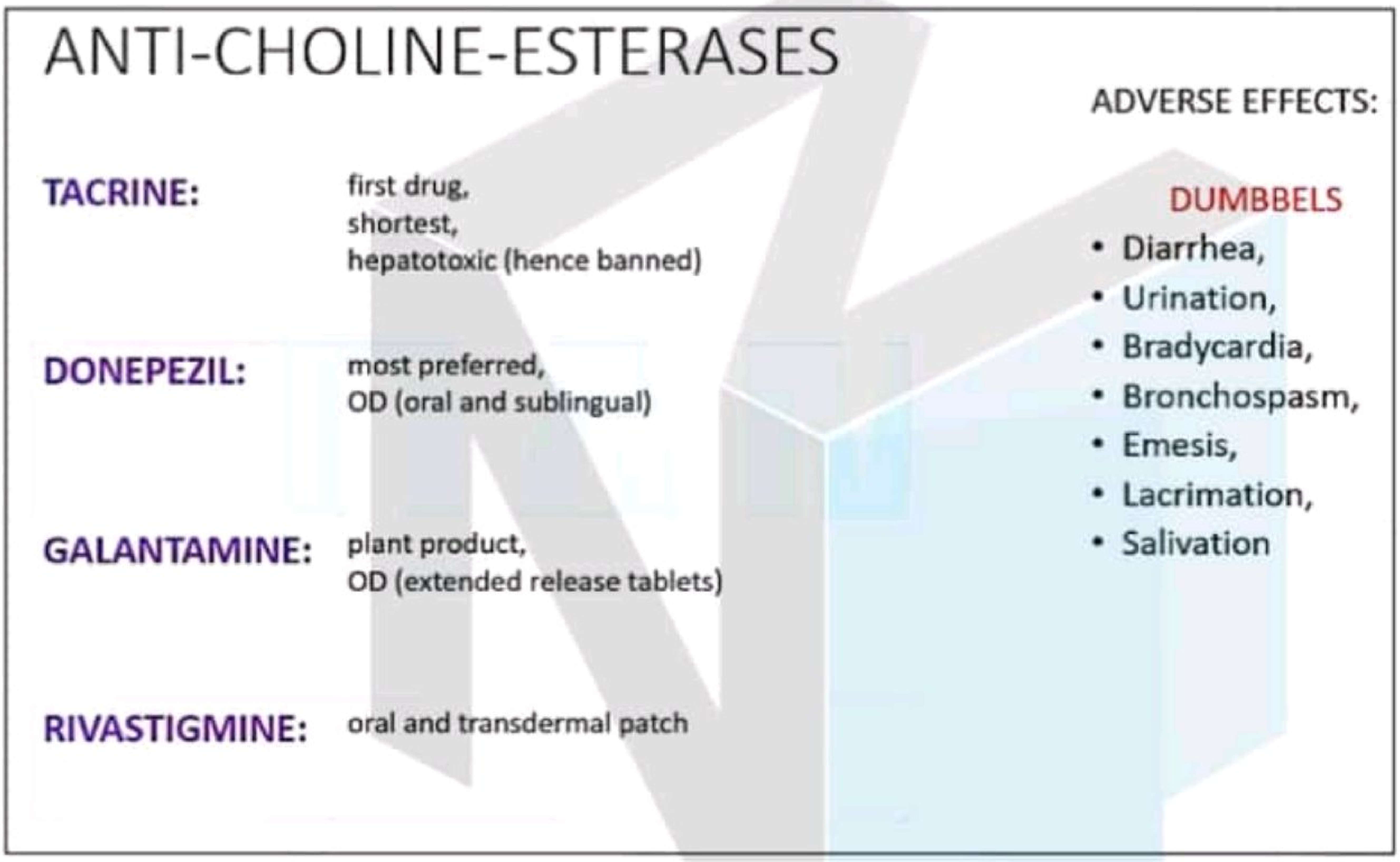
1. ANTI-CHOLINE-ESTERASES:

INCREASE ACETYL CHOLINE → IMPROVE COGNITION

↓

2. MEMANTINE:

- NMDA BLOCKER
- ADDED TO ANTI-CHOLINE-ESTERASES IN MODERATE – SEVERE DEMENTIA (MMSE < 18)
- OR IF PATIENT CANNOT TOLERATE ANTI-CHOLINE-ESTERASES



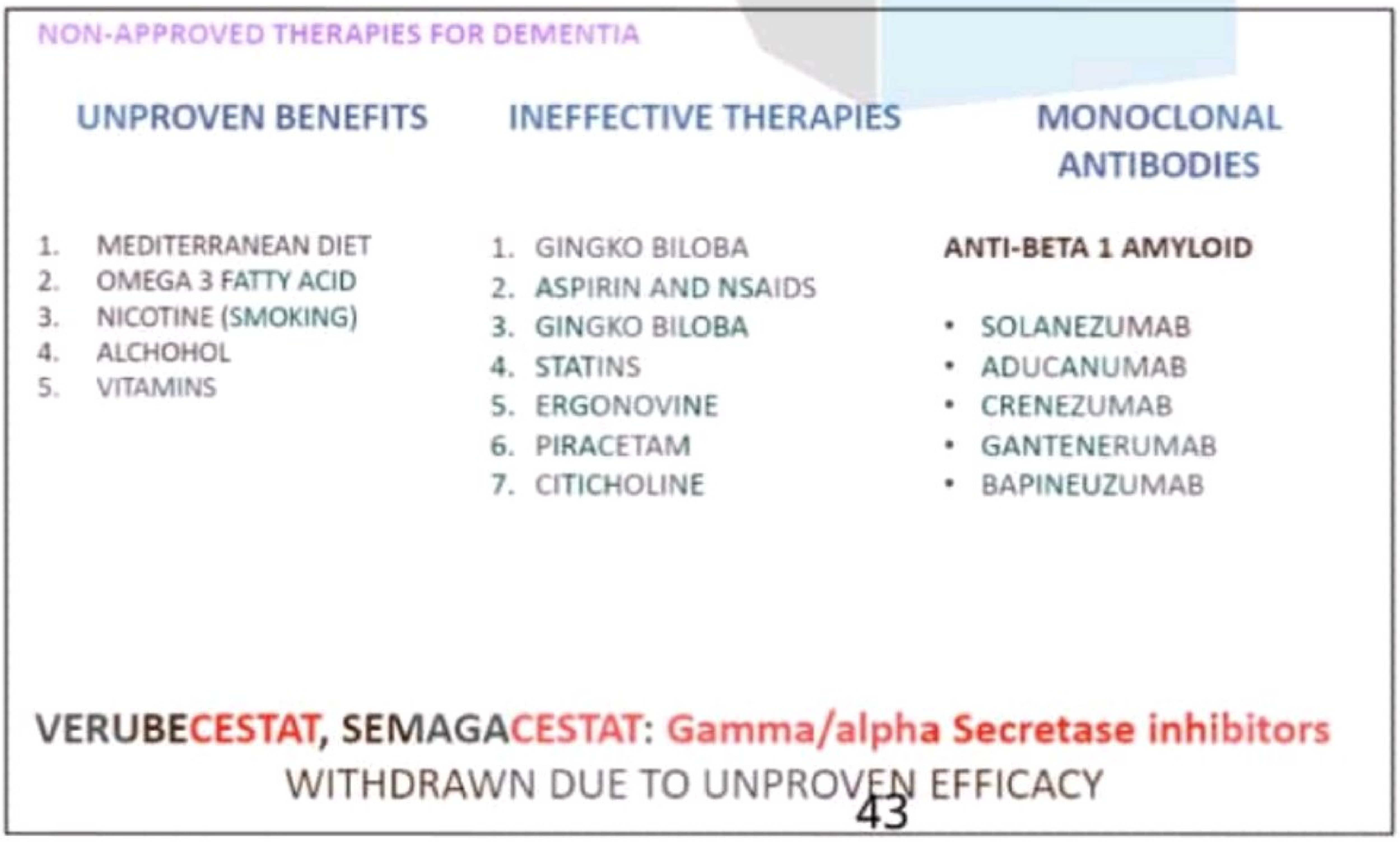
ANTI-CHOLINE-ESTERASES

TACRINE:	first drug, shortest, hepatotoxic (hence banned)
DONEPEZIL:	most preferred, OD (oral and sublingual)
GALANTAMINE:	plant product, OD (extended release tablets)
RIVASTIGMINE:	oral and transdermal patch

ADVERSE EFFECTS:

DUMBBELS

- Diarrhea,
- Urination,
- Bradycardia,
- Bronchospasm,
- Emesis,
- Lacrimation,
- Salivation



NON-APPROVED THERAPIES FOR DEMENTIA

UNPROVEN BENEFITS

1. MEDITERRANEAN DIET
2. OMEGA 3 FATTY ACID
3. NICOTINE (SMOKING)
4. ALCHOHOL
5. VITAMINS

INEFFECTIVE THERAPIES

1. GINGKO BILOBA
2. ASPIRIN AND NSAIDS
3. GINGKO BILOBA
4. STATINS
5. ERGONOVINE
6. PIRACETAM
7. CITICHOLINE

MONOCLONAL ANTIBODIES

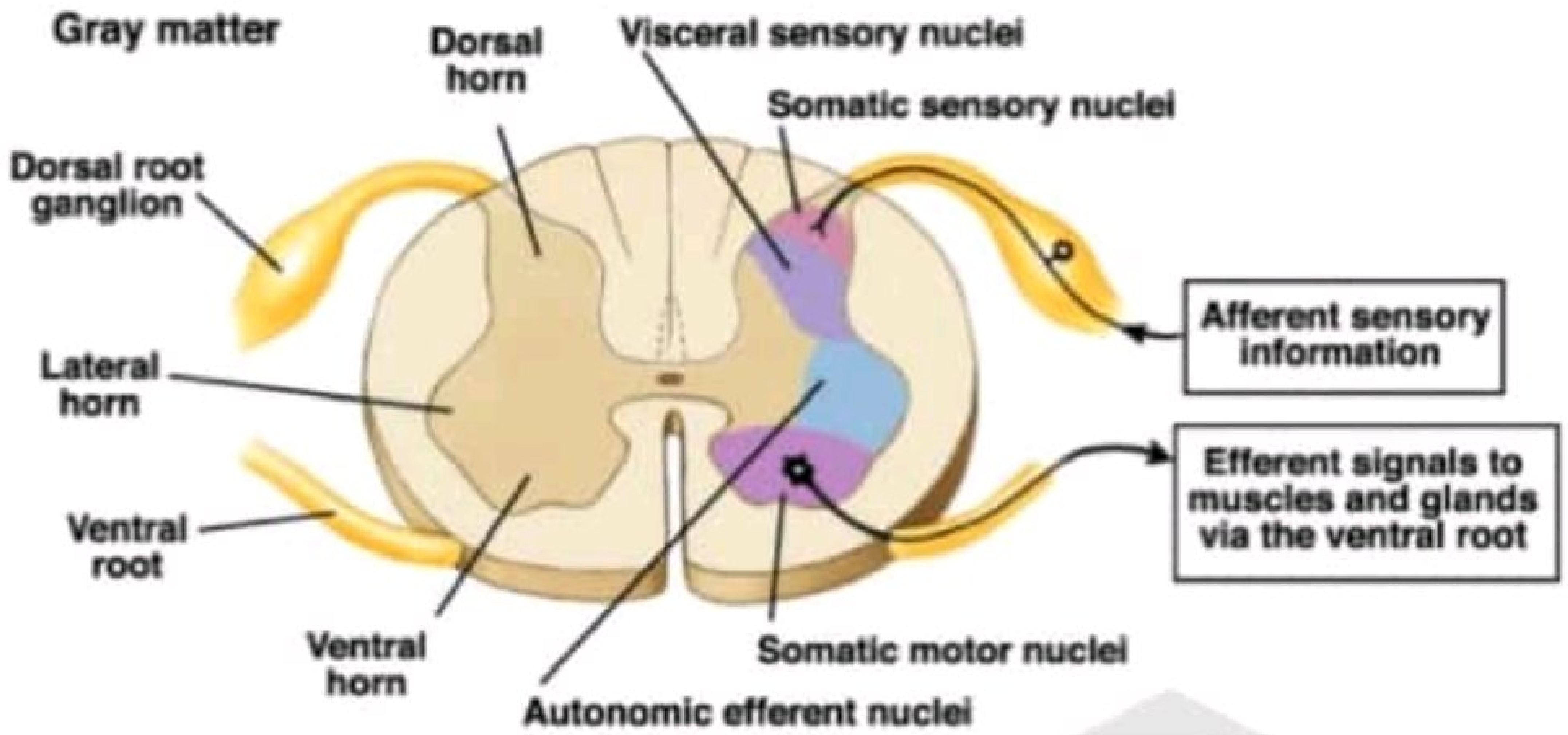
ANTI-BETA 1 AMYLOID

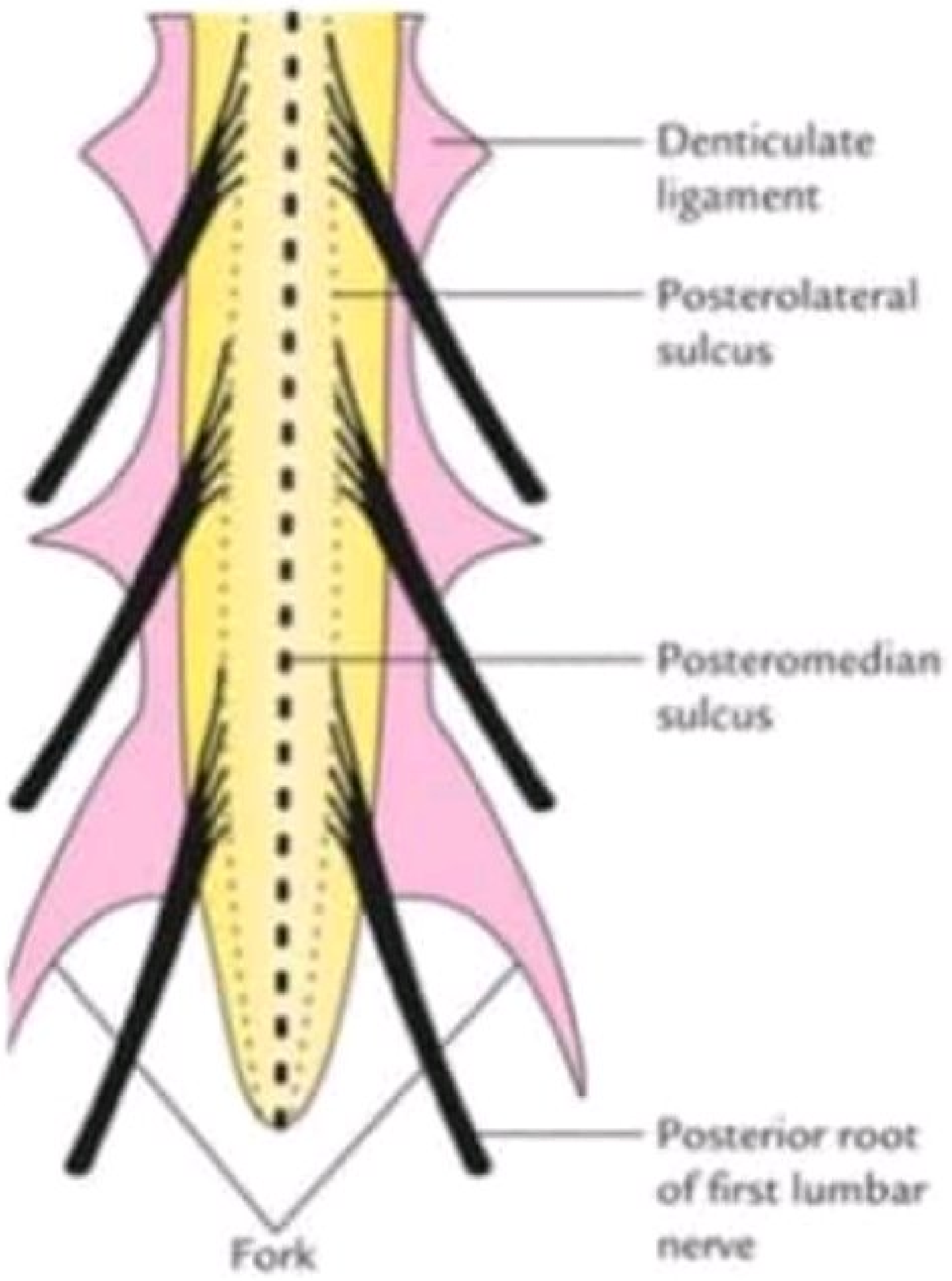
- SOLANEZUMAB
- ADUCANUMAB
- CRENEZUMAB
- GANTENERUMAB
- BAPINEUZUMAB

VERUBECESTAT, SEMAGACESTAT: Gamma/alpha Secretase inhibitors

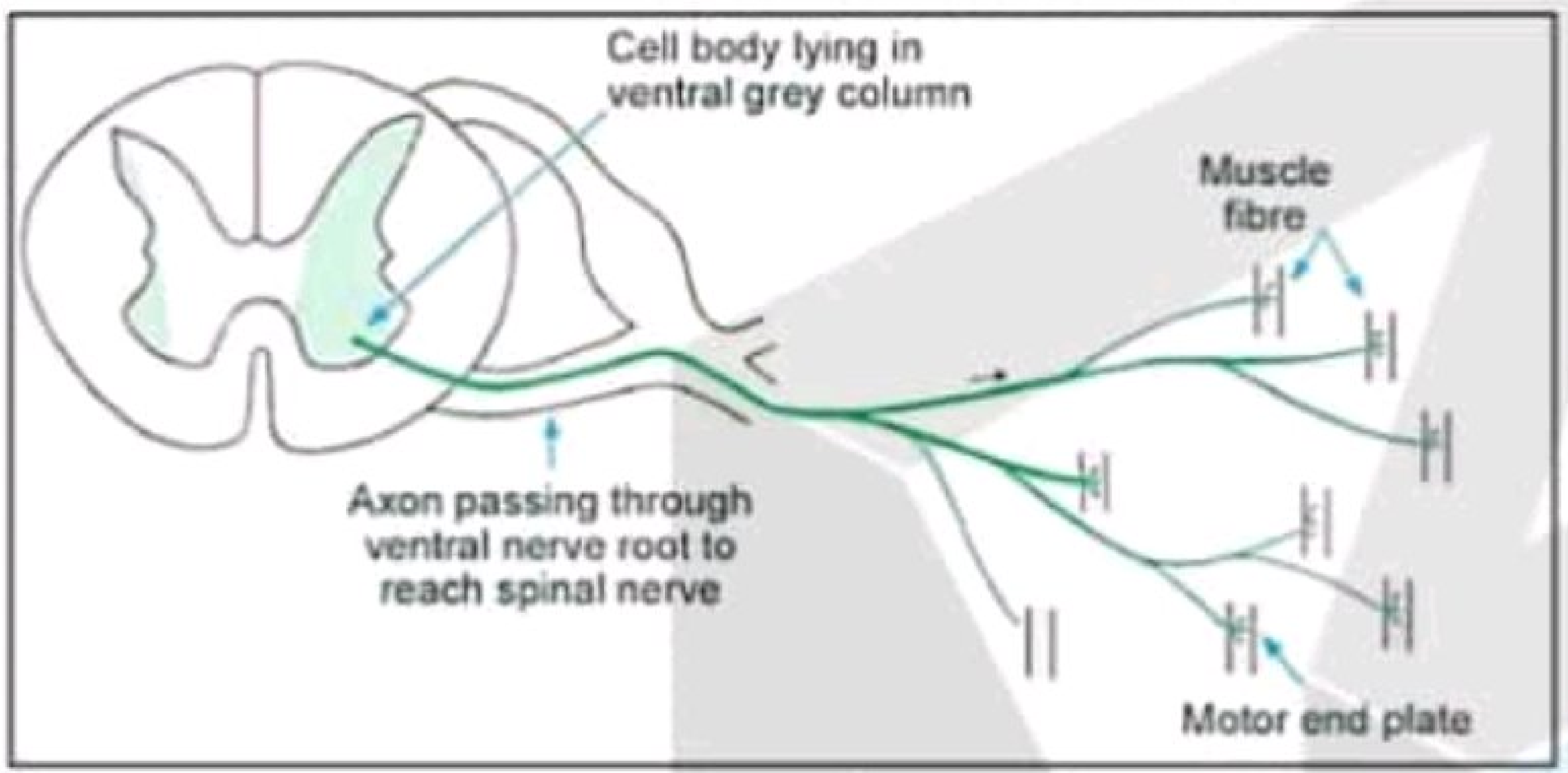
WITHDRAWN DUE TO UNPROVEN EFFICACY

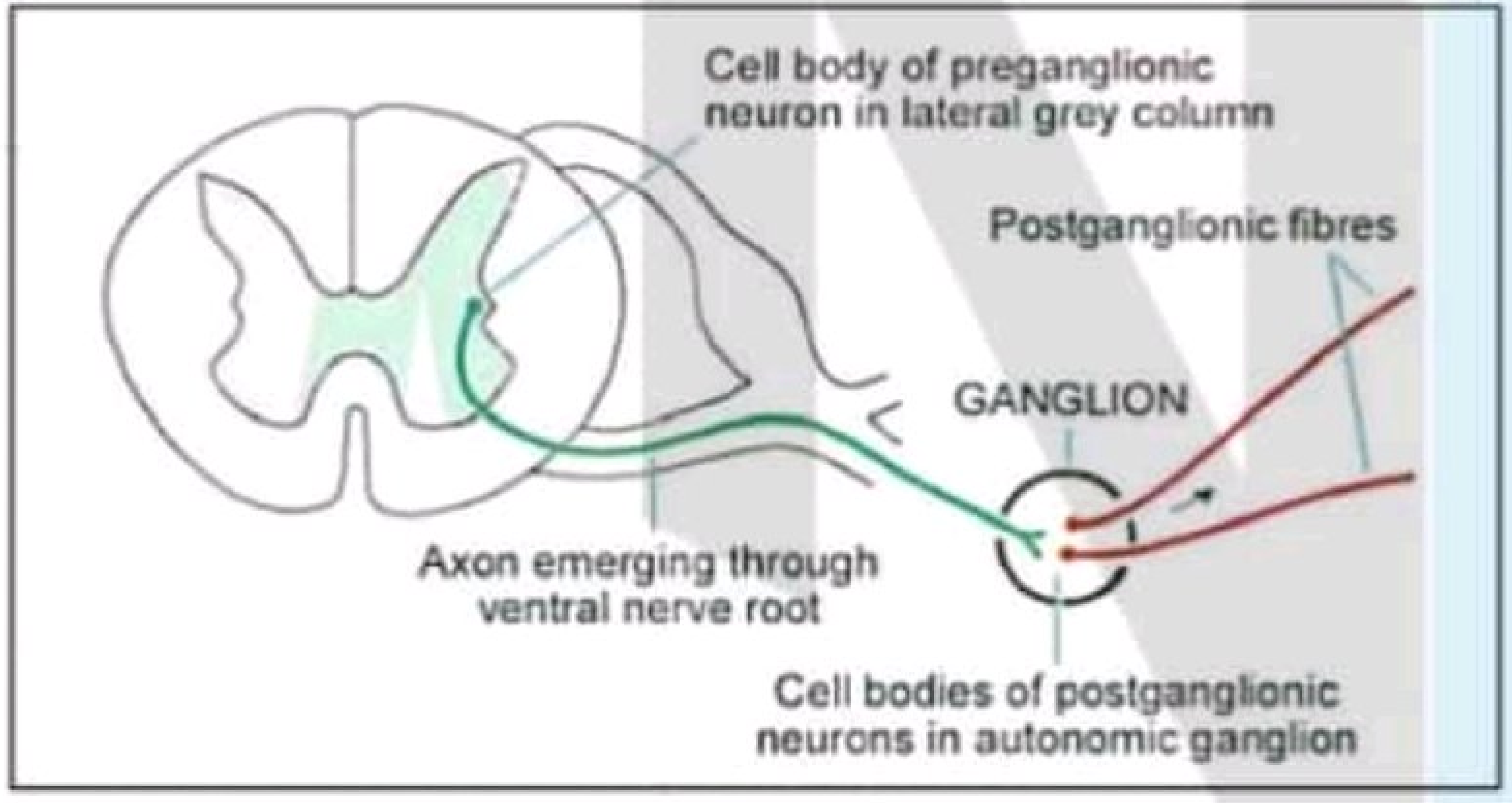
MYELOPATHY

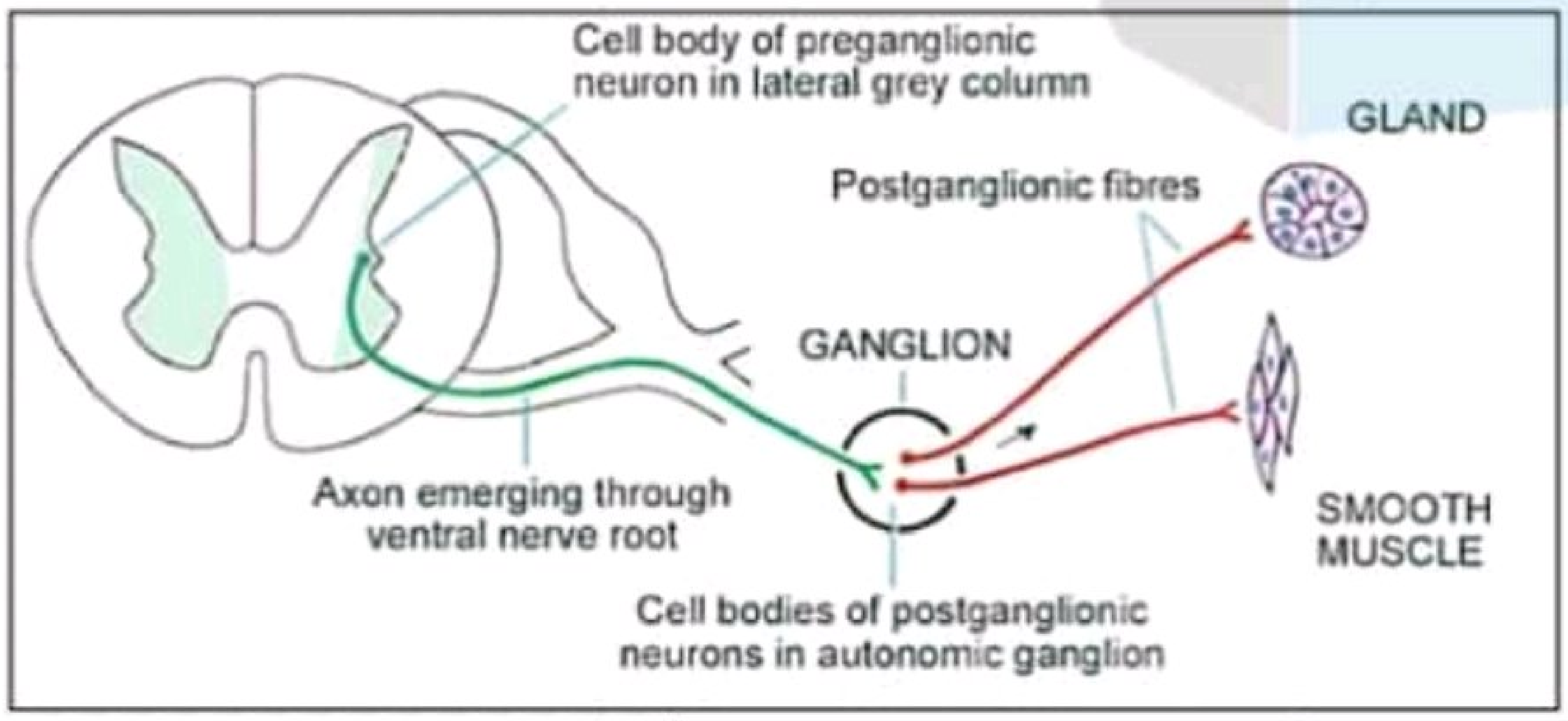

Gray matter
Dorsal horn
Visceral sensory nuclei
Somatic sensory nuclei
Dorsal root ganglion
Afferent sensory information
Lateral horn
Efferent signals to muscles and glands via the ventral root
Ventral root
Ventral horn
Somatic motor nuclei
Autonomic efferent nuclei

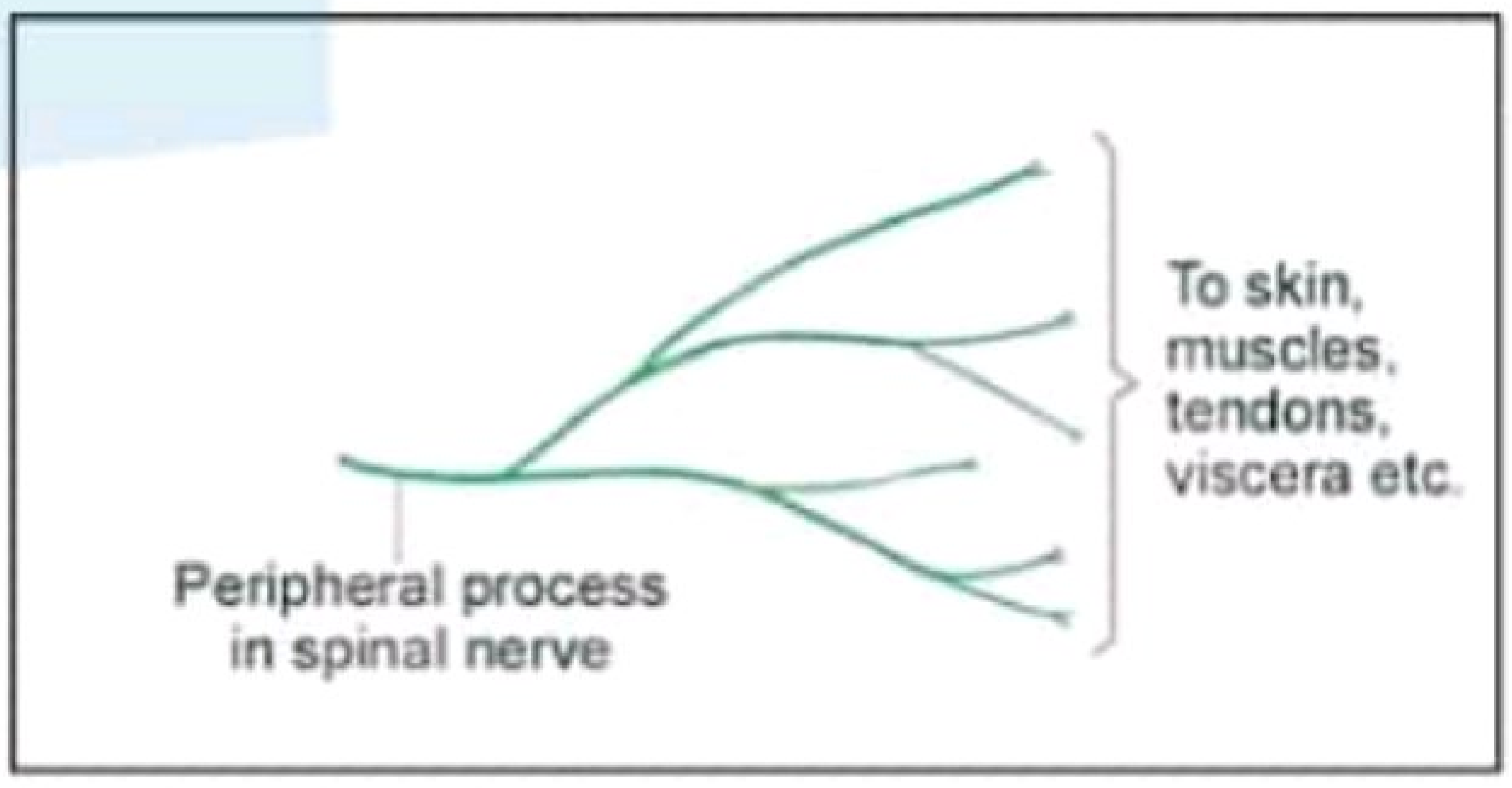

Denticulate ligament
Posterolateral sulcus
Posteromedian sulcus
Posterior root of first lumbar nerve
Fork

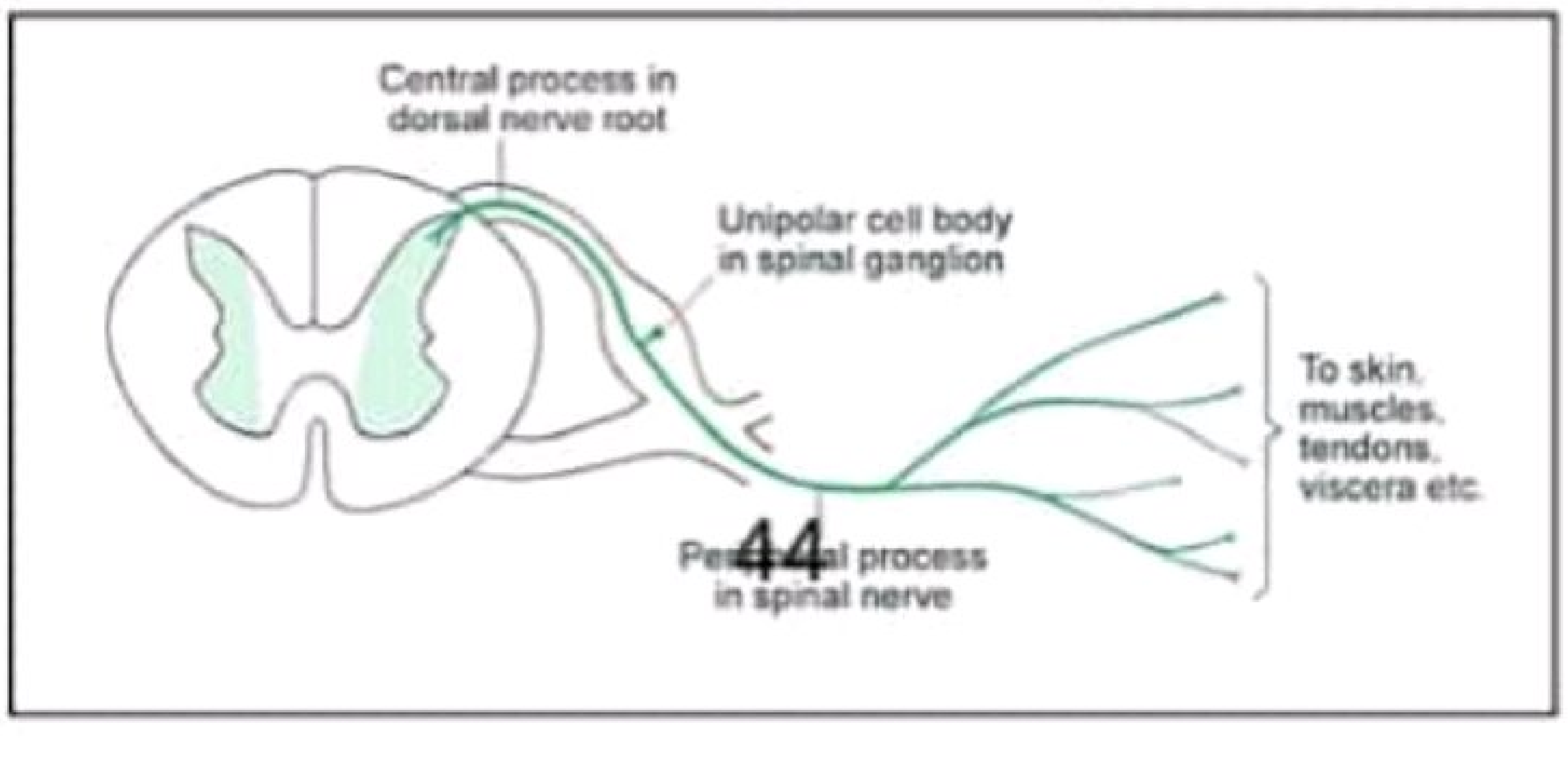
21 tooth like processes

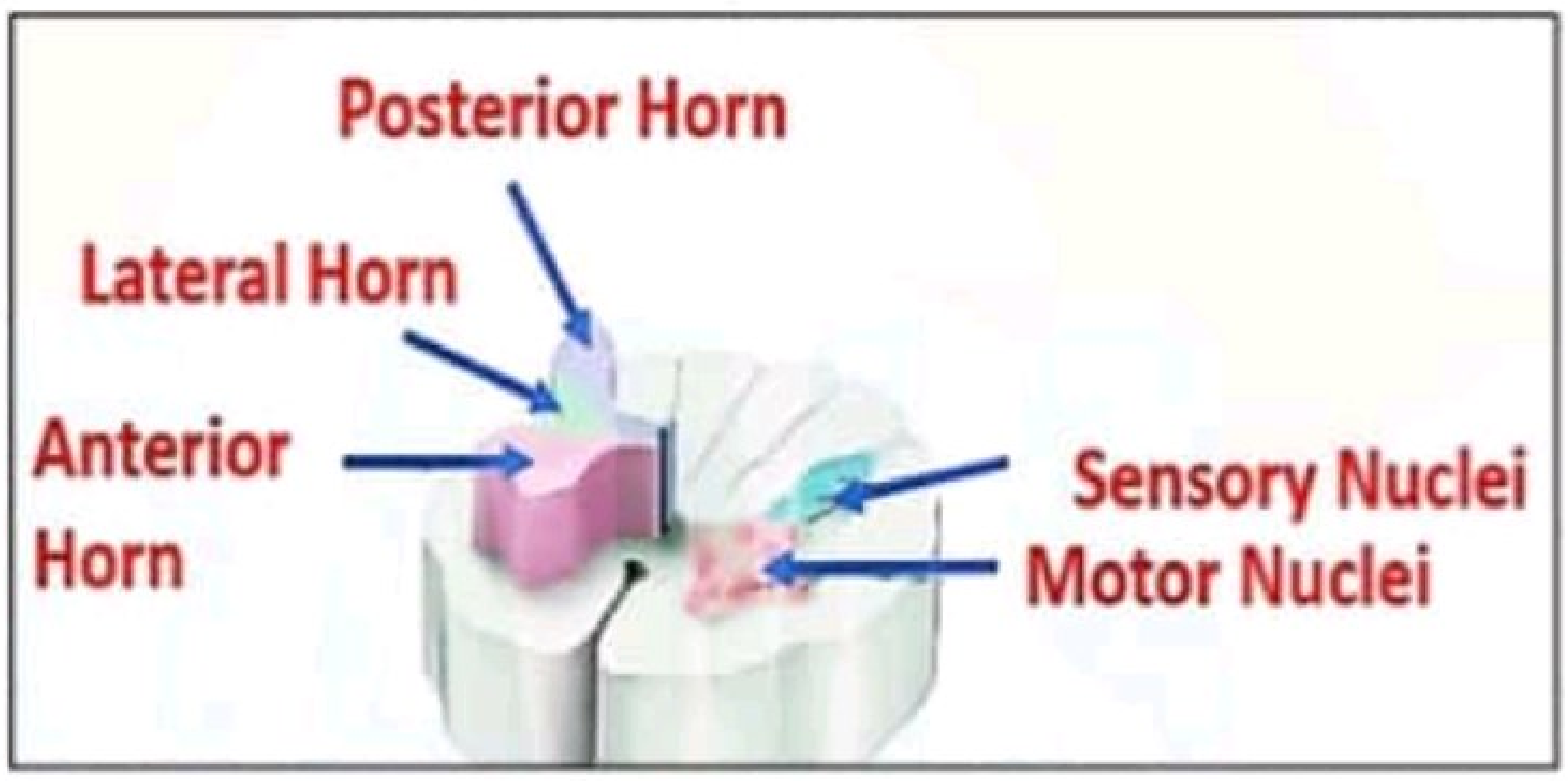

Cell body lying in ventral grey column
Muscle fibre
Axon passing through ventral nerve root to reach spinal nerve
Motor end plate

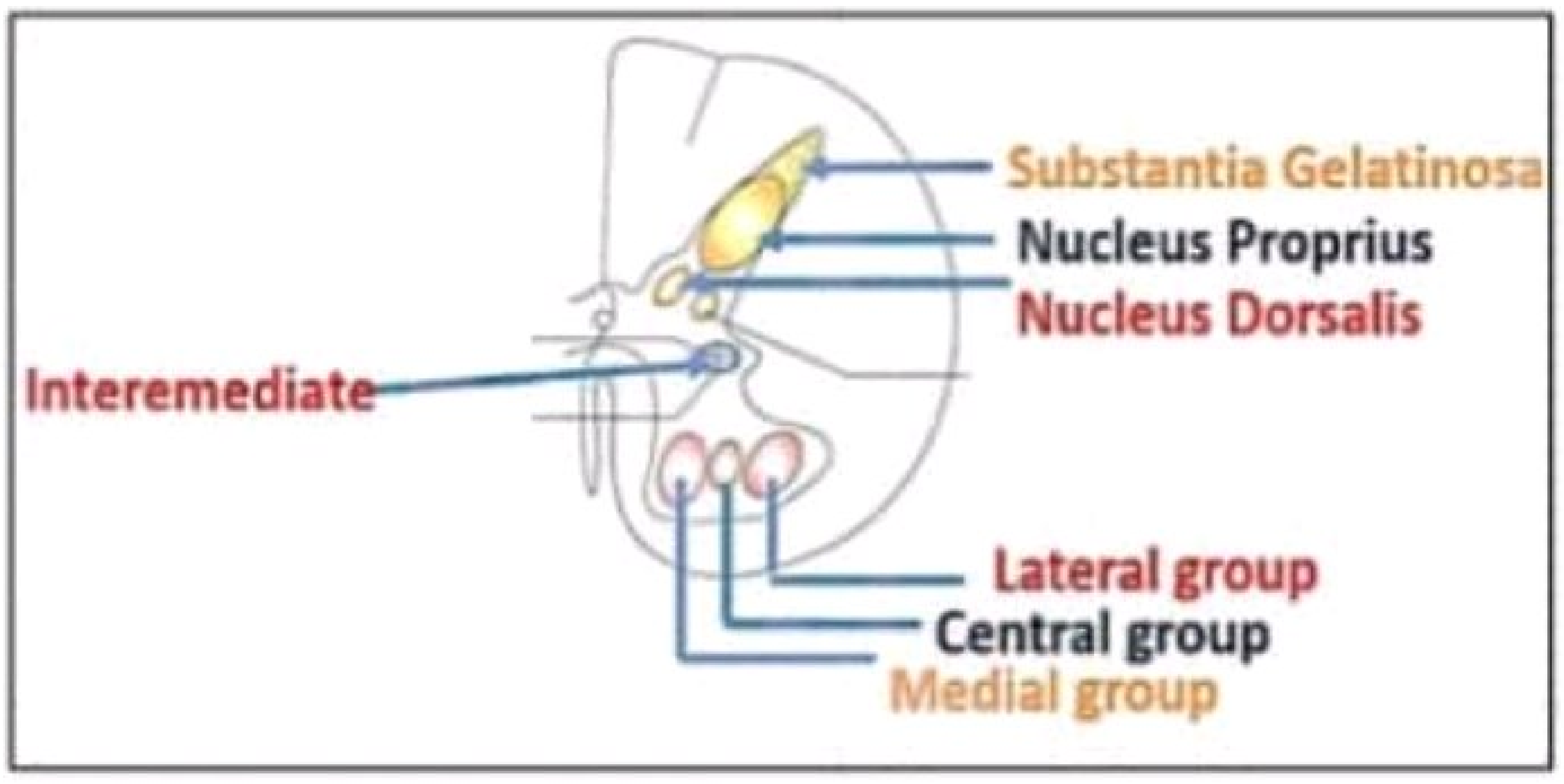

Cell body of preganglionic neuron in lateral grey column
Postganglionic fibres
GANGLION
Axon emerging through ventral nerve root
Cell bodies of postganglionic neurons in autonomic ganglion


Cell body of preganglionic neuron in lateral grey column
GLAND
Postganglionic fibres
GANGLION
Axon emerging through ventral nerve root
SMOOTH MUSCLE
Cell bodies of postganglionic neurons in autonomic ganglion


To skin, muscles, tendons, viscera etc.
Peripheral process in spinal nerve


Central process in dorsal nerve root
Unipolar cell body in spinal ganglion
To skin, muscles, tendons, viscera etc.
Peripheral process in spinal nerve


Posterior Horn
Lateral Horn
Anterior Horn
Sensory Nuclei
Motor Nuclei

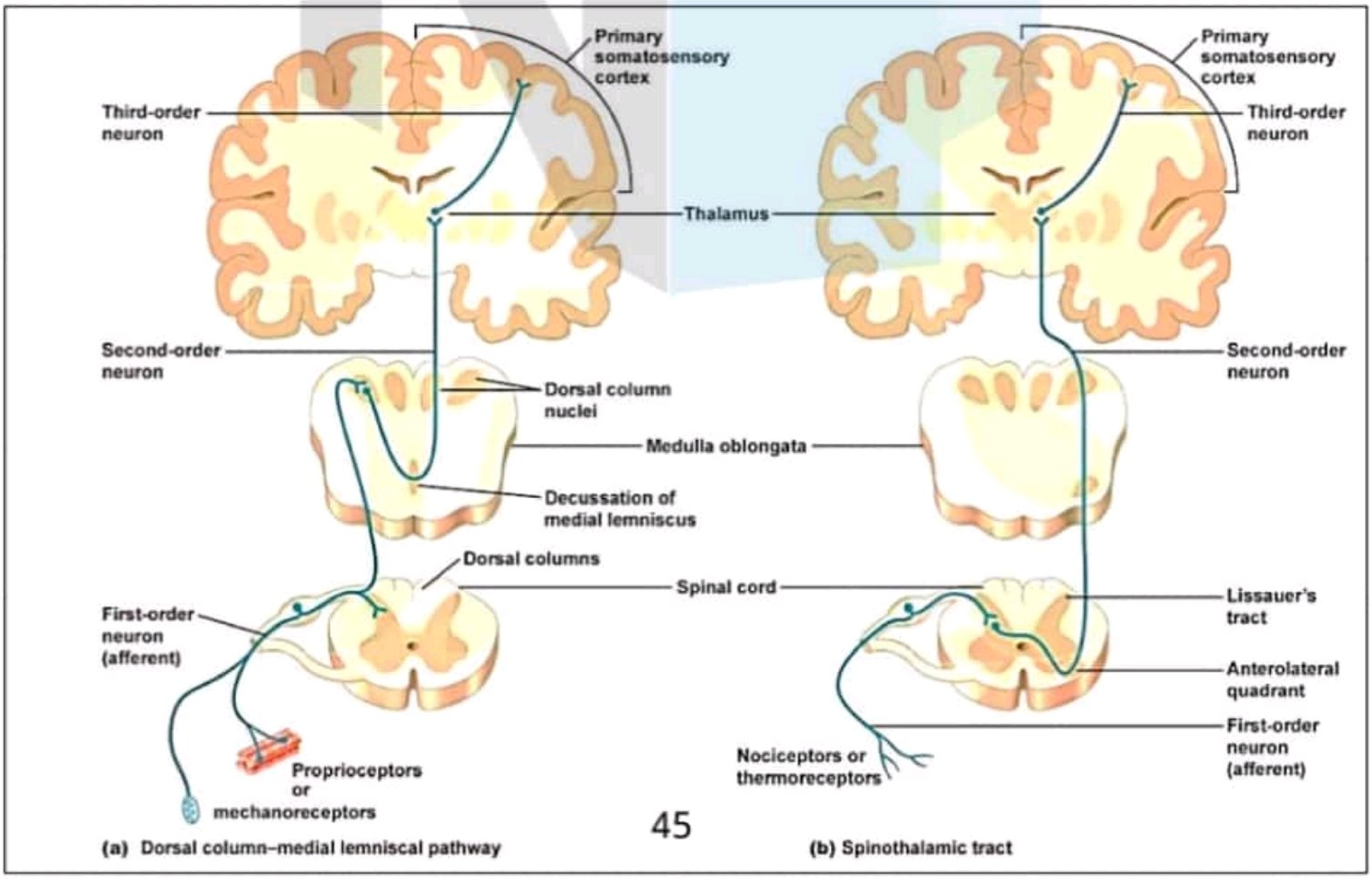

Substantia Gelatinosa
Nucleus Proprius
Nucleus Dorsalis
Interemediate
Lateral group
Central group
Medial group

Sensory/Ascending Tracts:

- Dorsal Column aka Dorsal Column Medial lemniscus system
    - Carries: Fine Touch, Conscious Proprioception, Localization, Two-point Discrimination, Vibration, Stereognosis.
- Spinothalamic tract
    - Lateral – Pain and temperature
    - Anterior – Crude Touch, Itch, Tickle, Sexual sensations

BAROGNOSIS – Pressure sensation→Ant ST; Change degrees in Pressure → Posterior ST tract

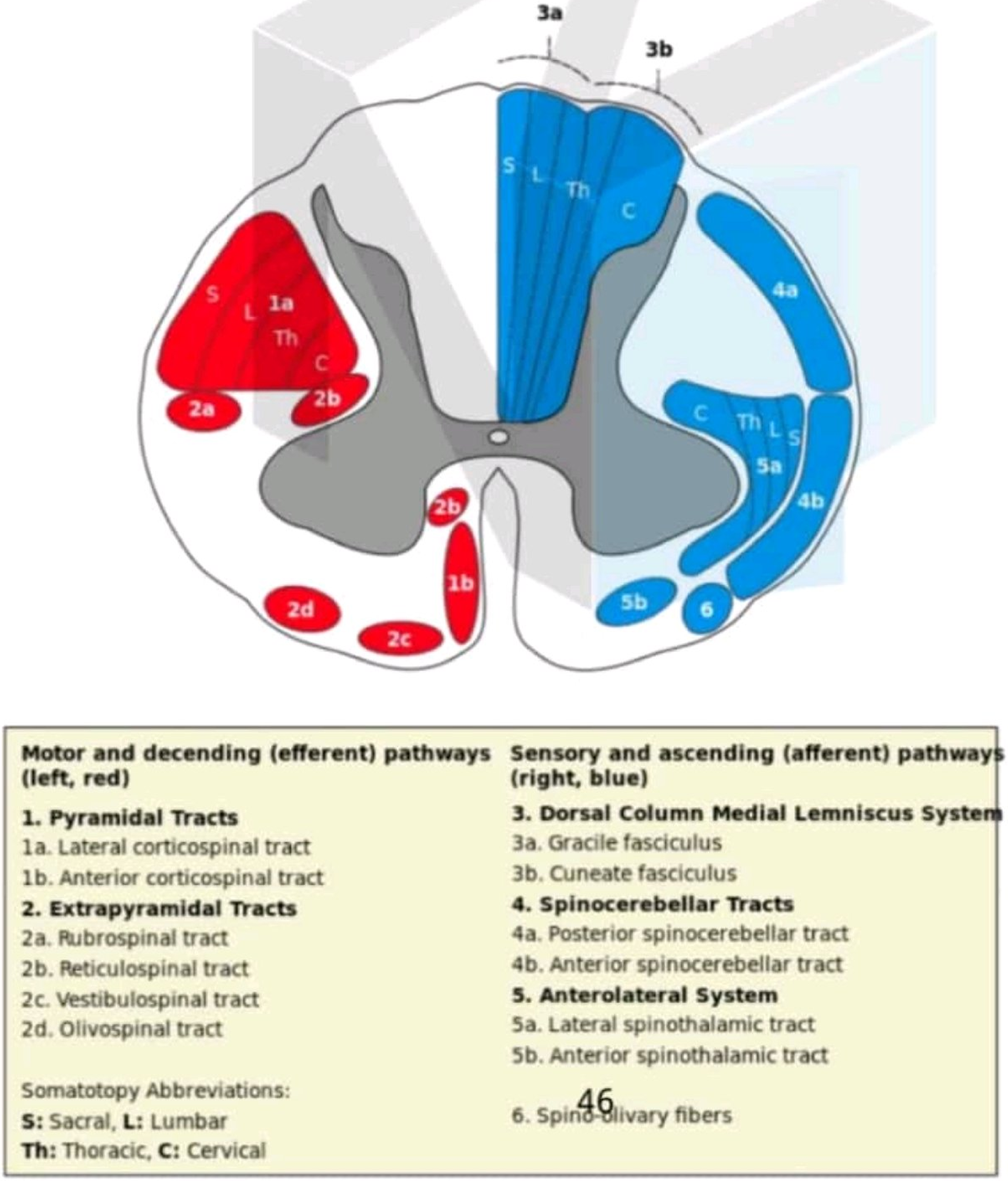
- Spinocerebellar tracts: Unconscious Proprioception
    - Anterior/Ventral (Gower's tract)- fibres from GTO
    - Posterior/dorsal (Flechsig's tract)- fibres from GTO & Muscle spindles
- ROSTRAL SPINOCEREBELLAR TRACT: fibres from GTO
  CUNEO SPINOCEREBELLAR TRACT: fibres from GTO & Muscle spindles


Primary somatosensory cortex
Third-order neuron
Thalamus
Second-order neuron
Dorsal column nuclei
Medulla oblongata
Decussation of medial lemniscus
Dorsal columns
Spinal cord
First-order neuron (afferent)
Proprioceptors or mechanoreceptors
Primary somatosensory cortex
Third-order neuron
Second-order neuron
Lissauer's tract
Anterolateral quadrant
First-order neuron (afferent)
Nociceptors or thermoreceptors

(a) Dorsal column–medial lemniscal pathway (b) Spinothalamic tract

IMPORTANT POINTS

- Dorsal Spinocerebellar tract is an uncrossed tract.
- Ventral Spinocerebellar tract crosses two times, henceforth reaches the ipsilateral cerebellum lobe.
- The 1st order neuron in both the spinothalamic tracts is the Dorsal Root Ganglion (DRG) (psuedounipolar)
- For Dorsal ST:
  - 2nd order neuron starts from **Nucleus Gracilis** and **Nucleus Cuneatus** in medulla
  - 3rd order neuron starts from **Ventral Postero-lateral nucleus** in Thalamus
- For Ventral ST: 3rd order neuron starts from **Ventral Postero-lateral nucleus** in Thalamus
- Gracile Fasciculus → Fibres of GOLL
- Cuneate Fasciculus → Fibres of BURDACH → Tract specific for STEREGONOSIS
- *Medullary Diseases will cause DESCENDING SENSORY loss*
- *Extra-Medullary Diseases will cause ASCENDING sensory loss*



Motor and decending (efferent) pathways (left, red)

1. Pyramidal Tracts
1a. Lateral corticospinal tract
1b. Anterior corticospinal tract

2. Extrapyramidal Tracts
2a. Rubrospinal tract
2b. Reticulospinal tract
2c. Vestibulospinal tract
2d. Olivospinal tract

Somatotopy Abbreviations:
S: Sacral, **L:** Lumbar
Th: Thoracic, **C:** Cervical

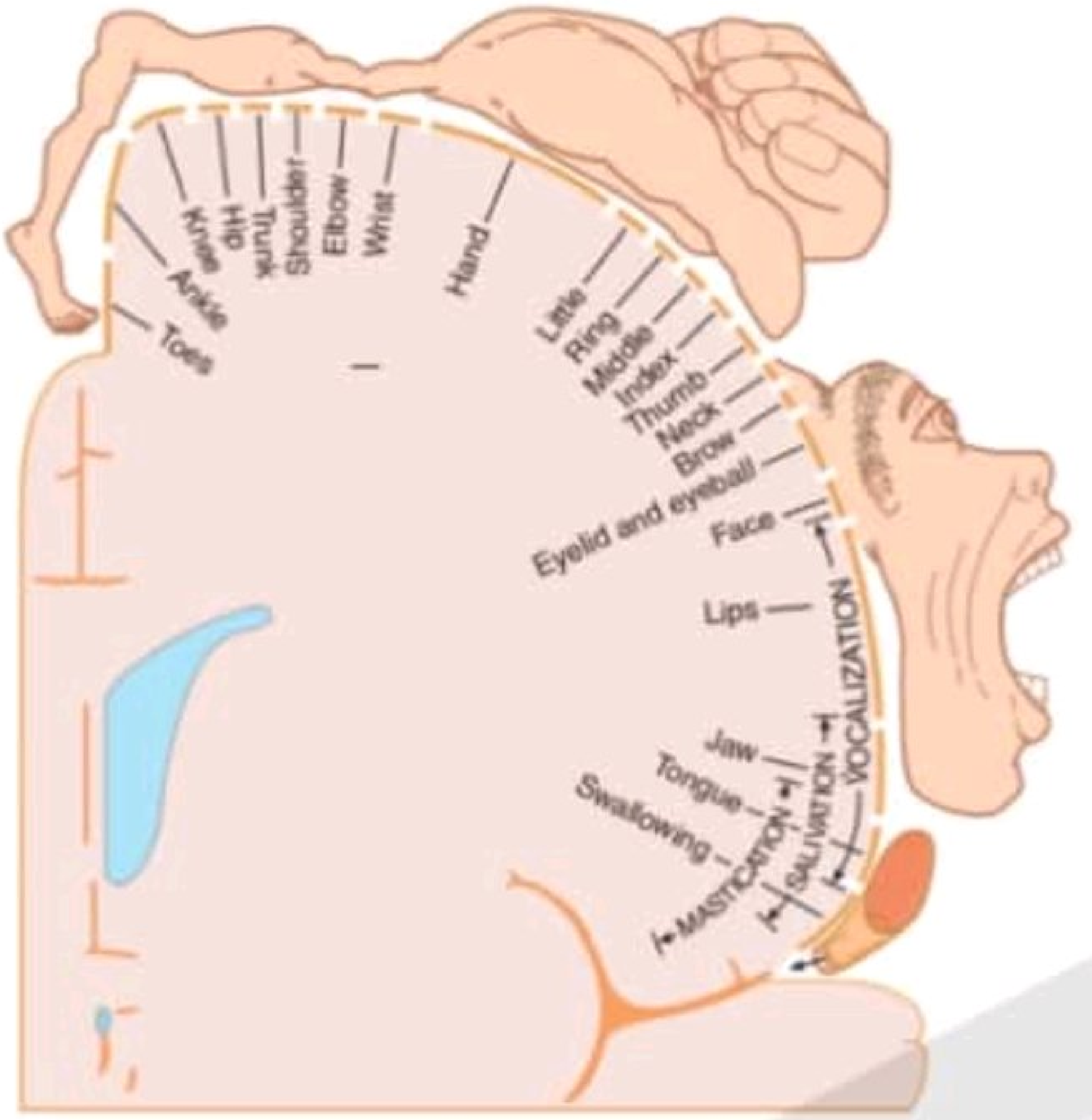
Sensory and ascending (afferent) pathways (right, blue)

3. Dorsal Column Medial Lemniscus System
3a. Gracile fasciculus
3b. Cuneate fasciculus

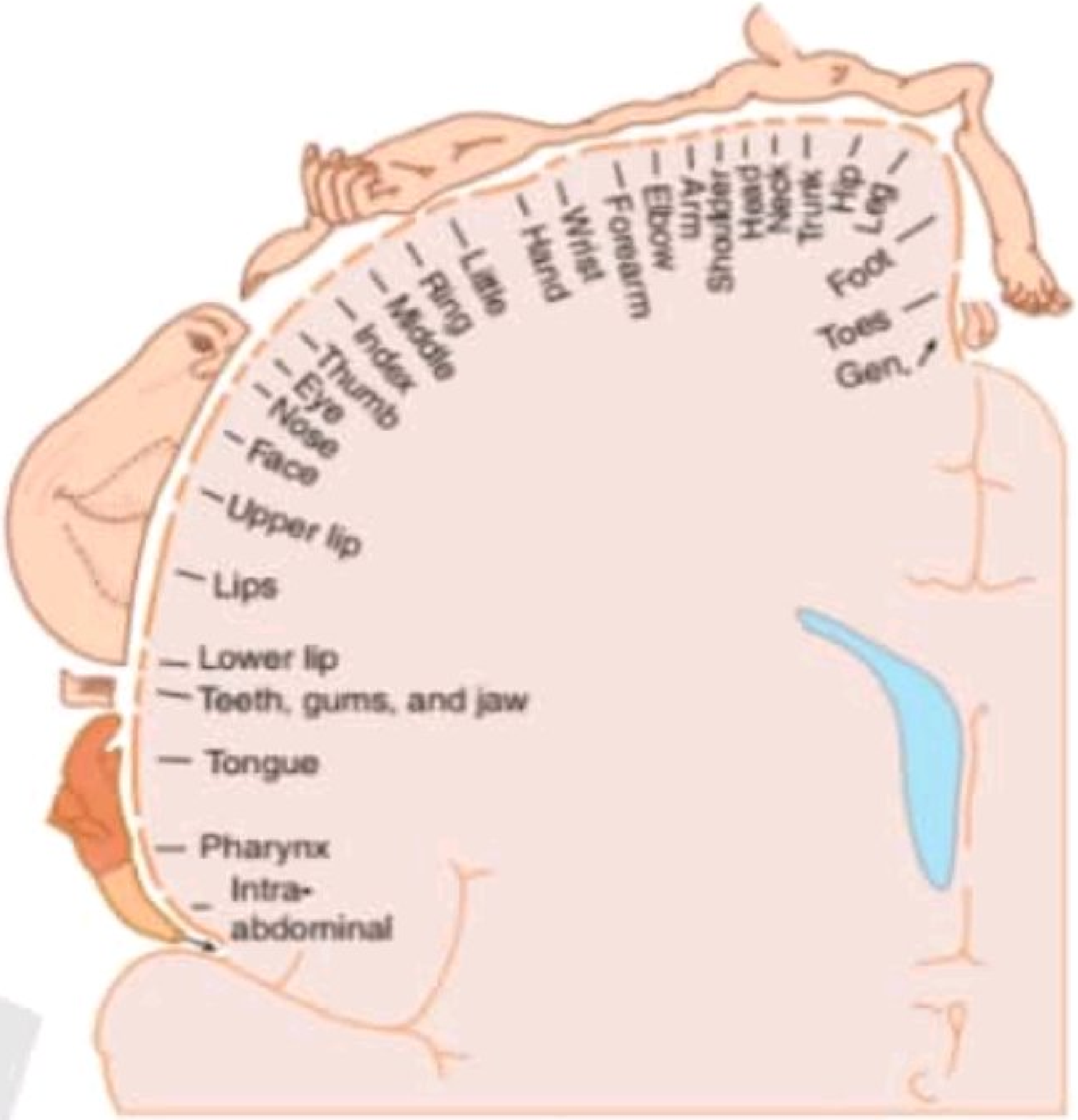
4. Spinocerebellar Tracts
4a. Posterior spinocerebellar tract
4b. Anterior spinocerebellar tract

5. Anterolateral System
5a. Lateral spinothalamic tract
5b. Anterior spinothalamic tract

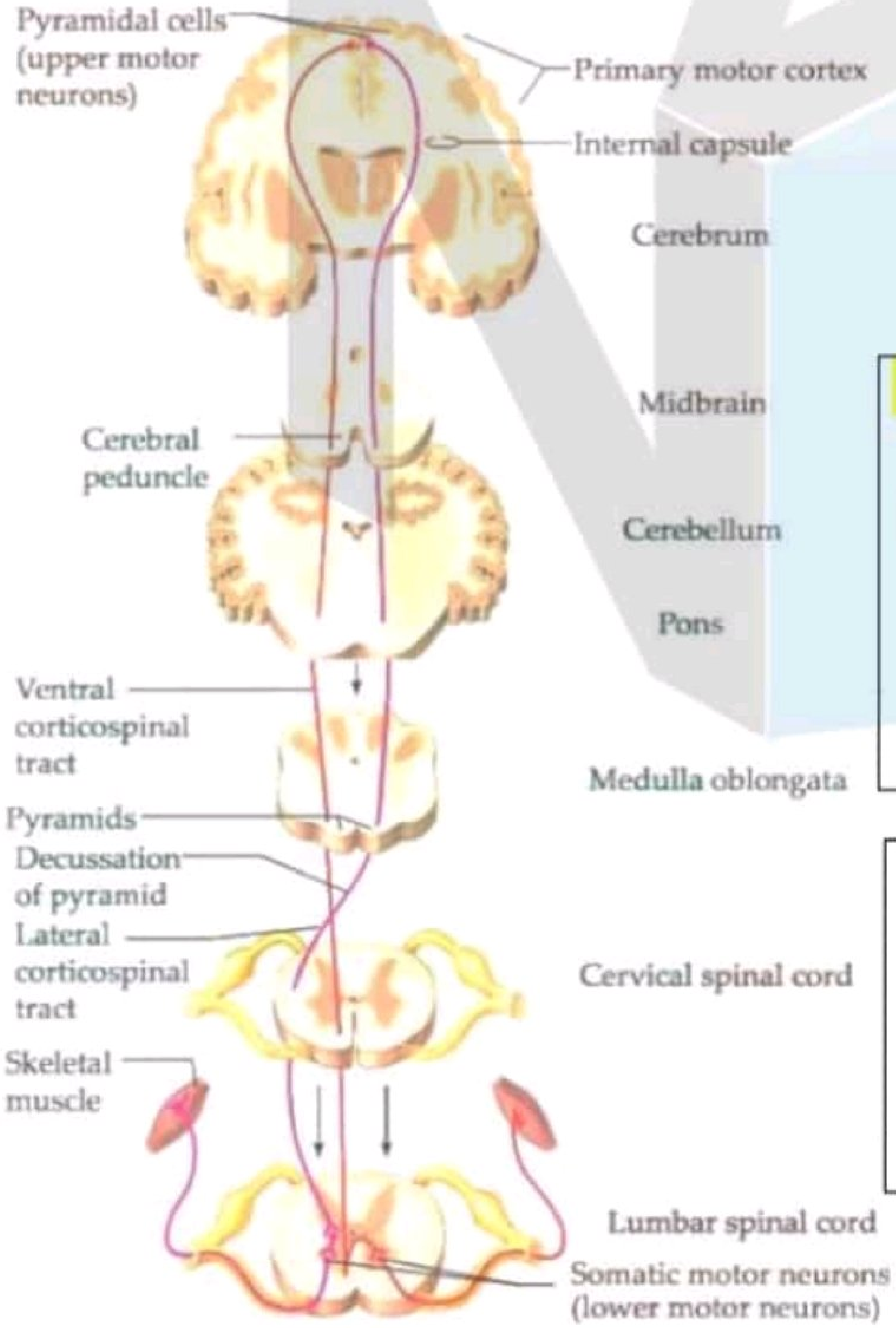
6. Spino-olivary fibers


Toes
Ankle
Knee
Hip
Trunk
Shoulder
Elbow
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Neck
Brow
Eyelid and eyeball
Face
Lips
Jaw
Tongue
Swallowing
MASTICATION
SALIVATION
VOCALIZATION

MOTOR HOMUNCULUS


Little
Ring
Middle
Index
Thumb
Eye
Nose
Face
Upper lip
Lips
Lower lip
Teeth, gums, and jaw
Tongue
Pharynx
Intra-abdominal
Hand
Wrist
Forearm
Elbow
Arm
Shoulder
Head
Neck
Trunk
Hip
Leg
Foot
Toes
Gen.

SENSORY HOMUNCULUS


Pyramidal cells (upper motor neurons)
Primary motor cortex
Internal capsule
Cerebrum
Midbrain
Cerebral peduncle
Cerebellum
Pons
Ventral corticospinal tract
Medulla oblongata
Pyramids
Decussation of pyramid
Lateral corticospinal tract
Cervical spinal cord
Skeletal muscle
Lumbar spinal cord
Somatic motor neurons (lower motor neurons)

Descending tracts (motor pathways)

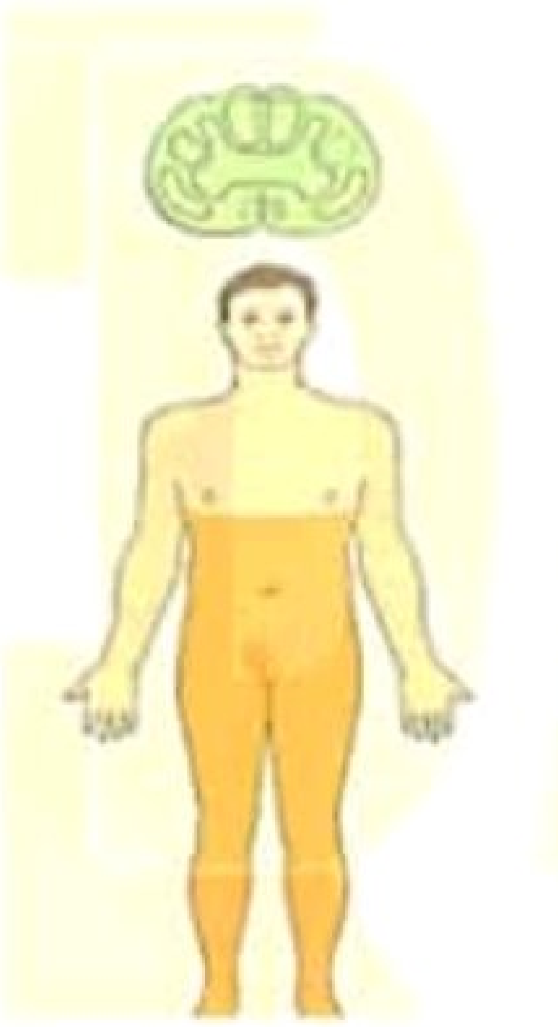
Medial Descending tracts	Lateral Descending tracts
1. Anterior corticospinal tract	1. Lateral corticospinal tract
2. Vestibulospinal tract	2. Rubrospinal tract
3. Tectospinal tract	
4. Reticulospinal tract • Pontine/ Excitatory • Medullary/ Inhibitory	

Origin

- Primary motor cortex
- Premotor and supplementary motor cortex
- Sensory cortex

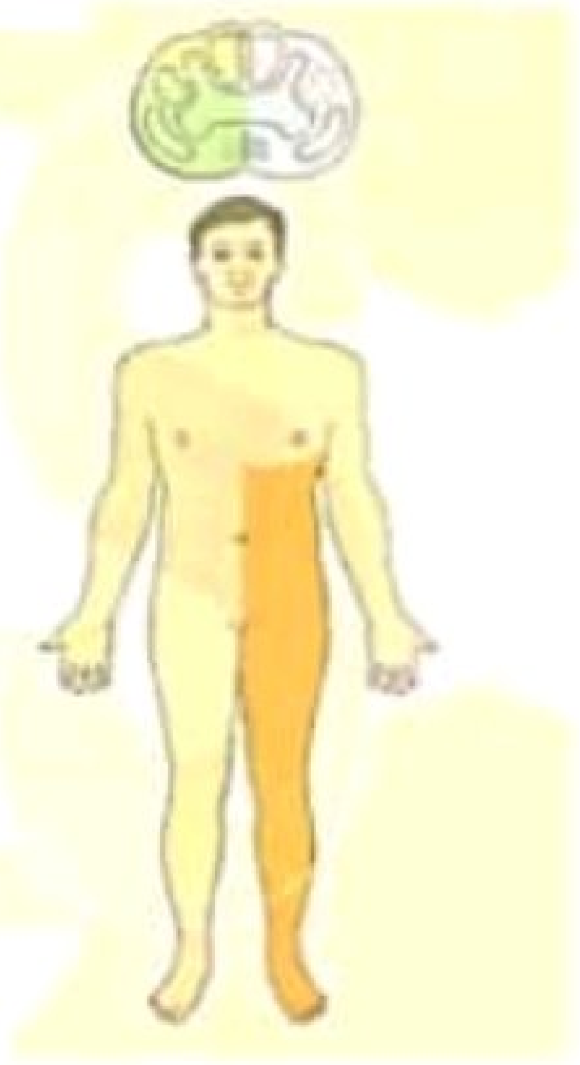
SENSORY LOSS IN MYELOPATHY

TRANSVERSE MYELITIS



ST –Impaired
PC –Impaired

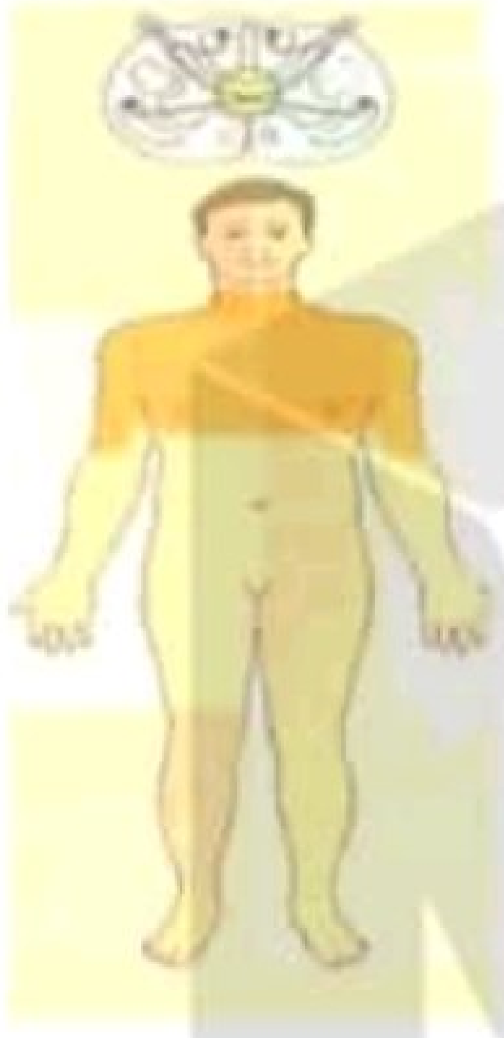
BROWN SEQUARD SYNDROME



ST –Intact
PC –Impaired

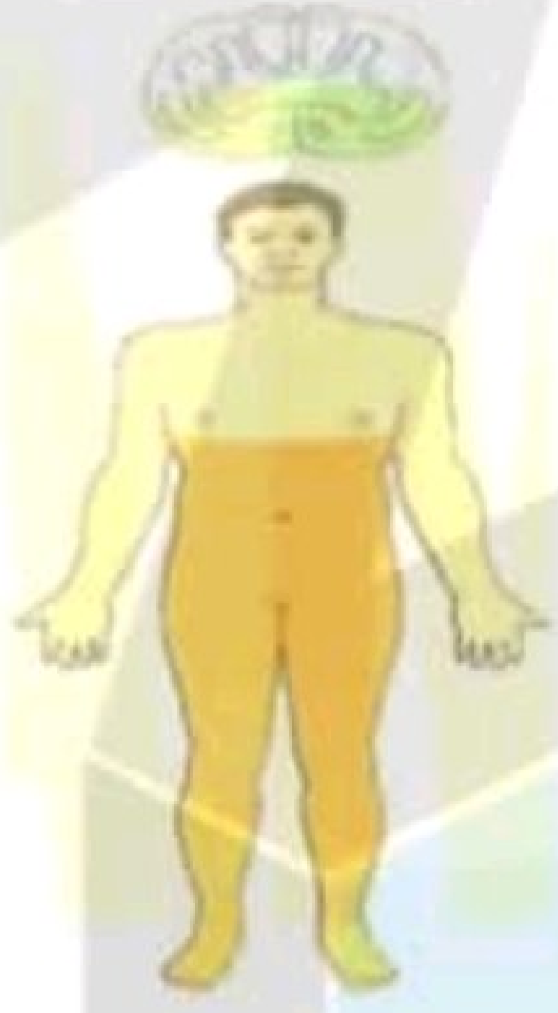
ST –Impaired
PC -Intact

SYRINGOMYELIA



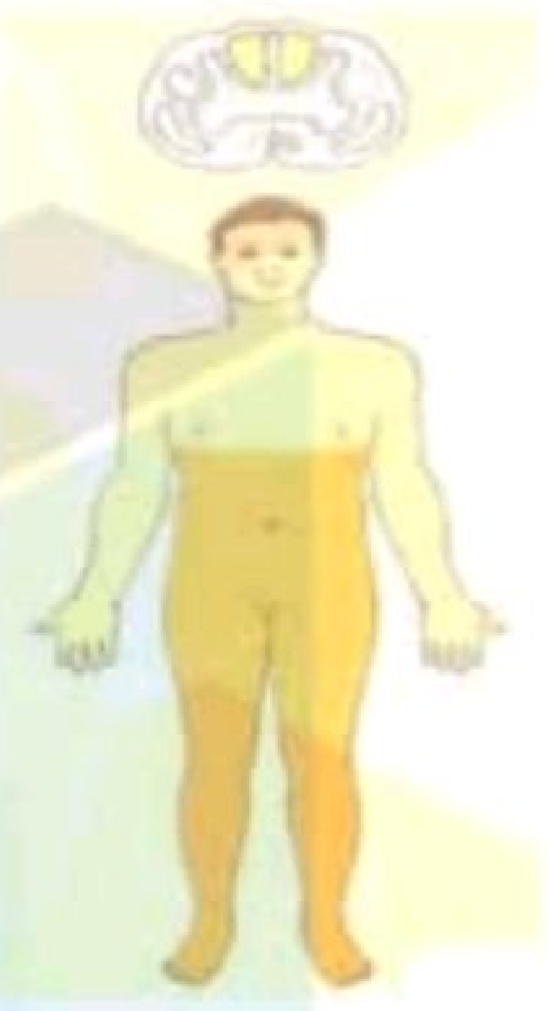
ST –Impaired
PC –Intact

ANTERIOR SPINAL ARTERY OCCLUSION



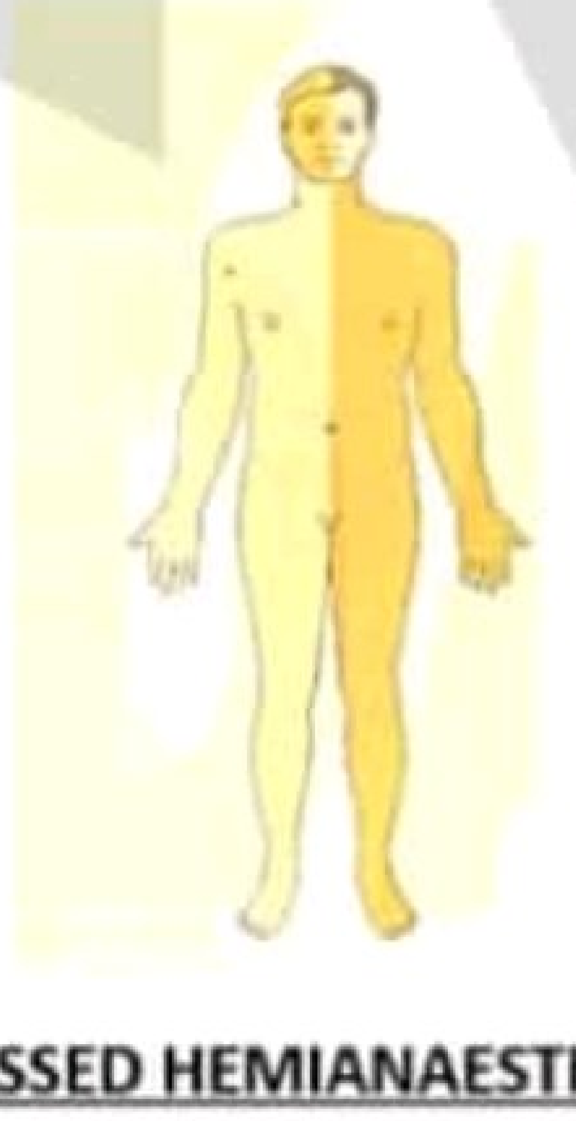
ST –Impaired
PC –Intact

TABES DORSALIS

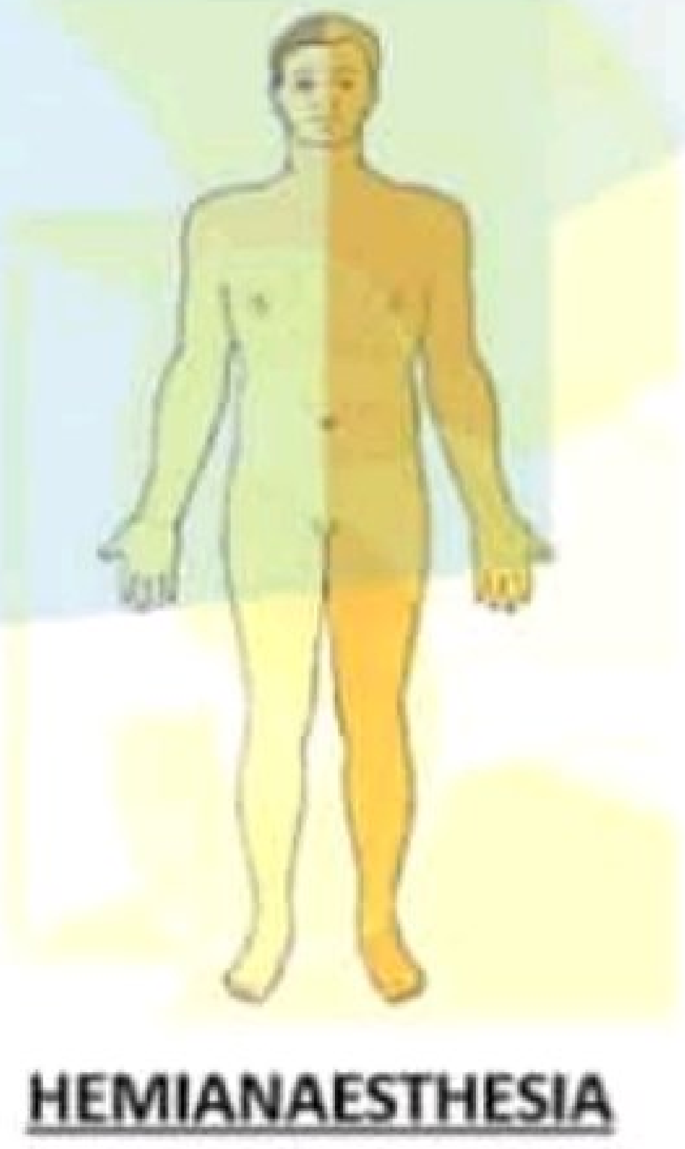


ST –Intact
PC –Impaired

ST –Impaired
PC –Impaired

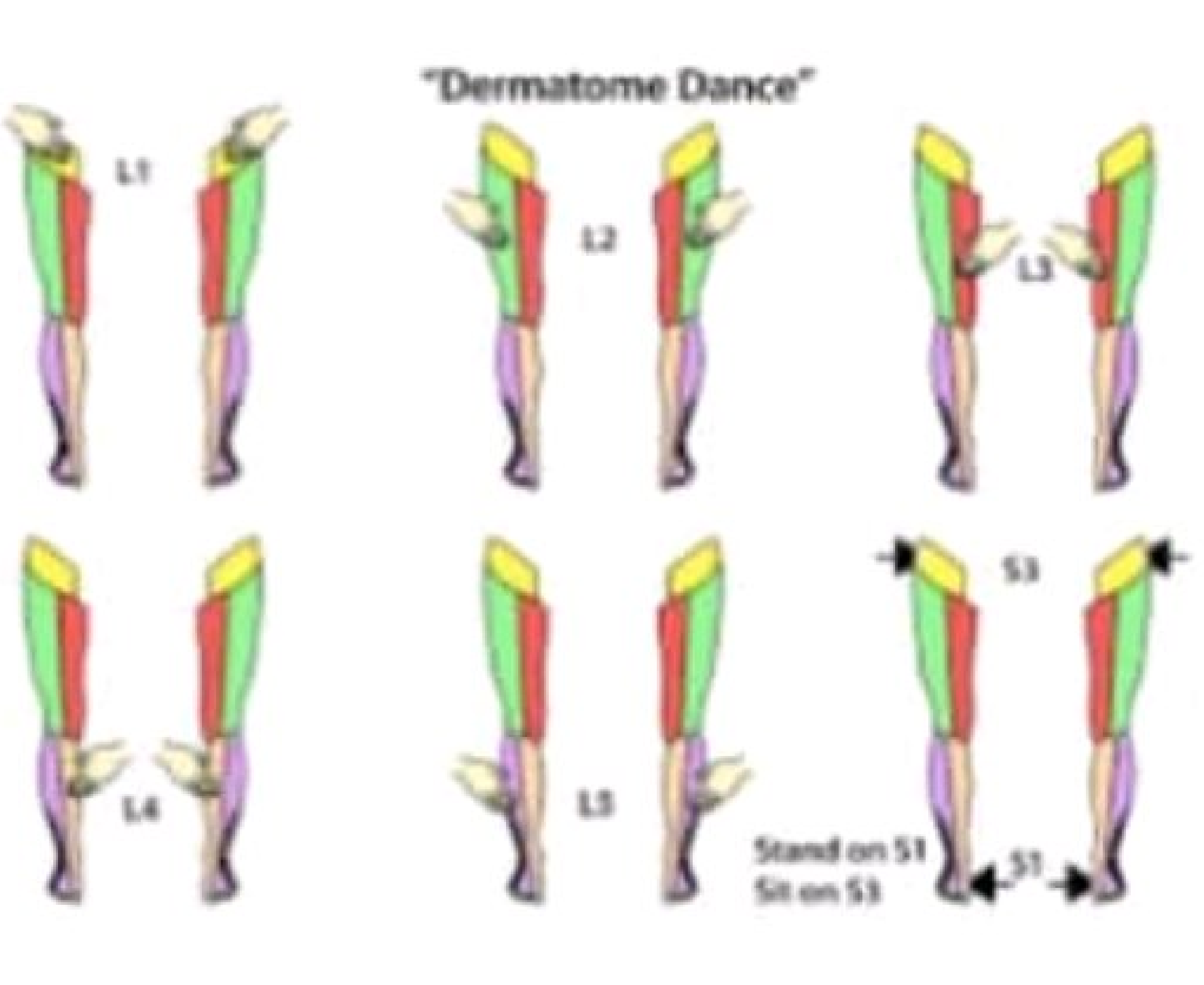


CROSSED HEMIANAESTHESIA
(LATERAL MEDULLARY LESION)



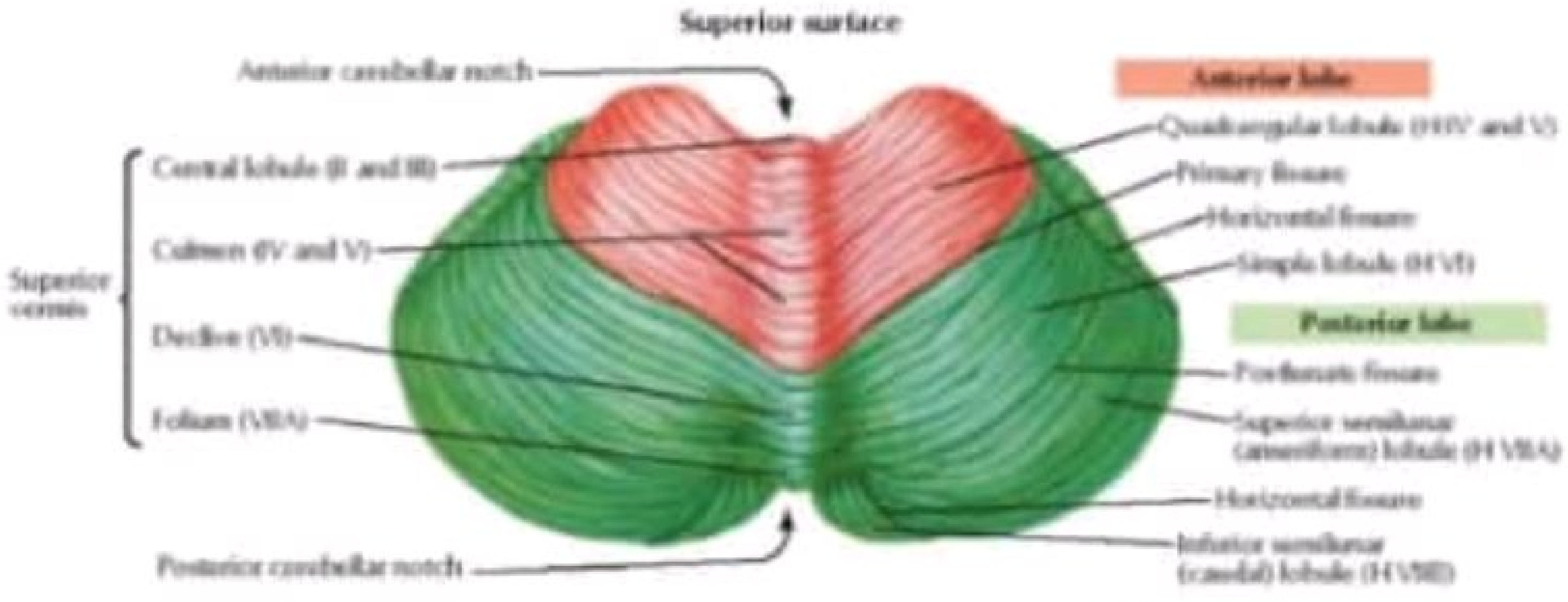
ST –Impaired
PC –Impaired

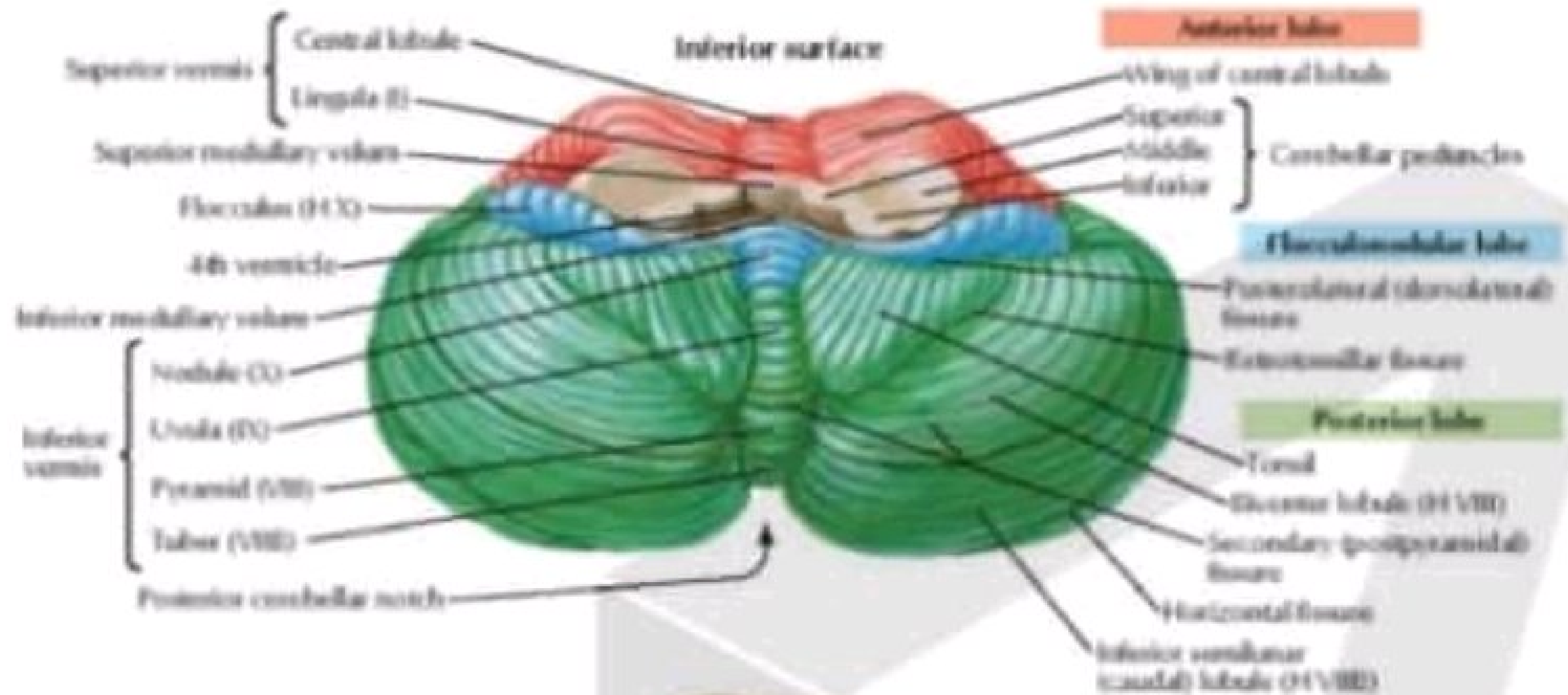
HEMIANAESTHESIA
(THALAMIC LESION)

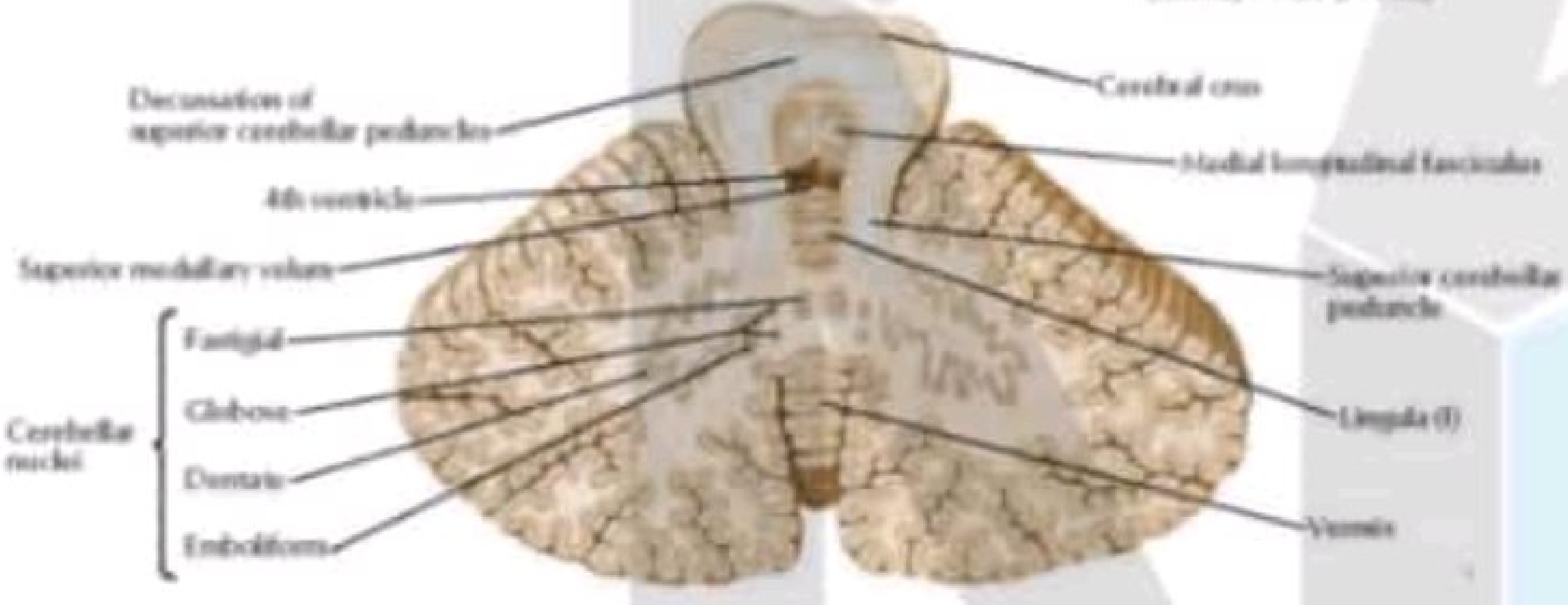

"Dermatome Dance"
L1
L2
L3
L4
L5
S3
Stand on S1
Sit on S3
S1

ATAXIC DISORDERS

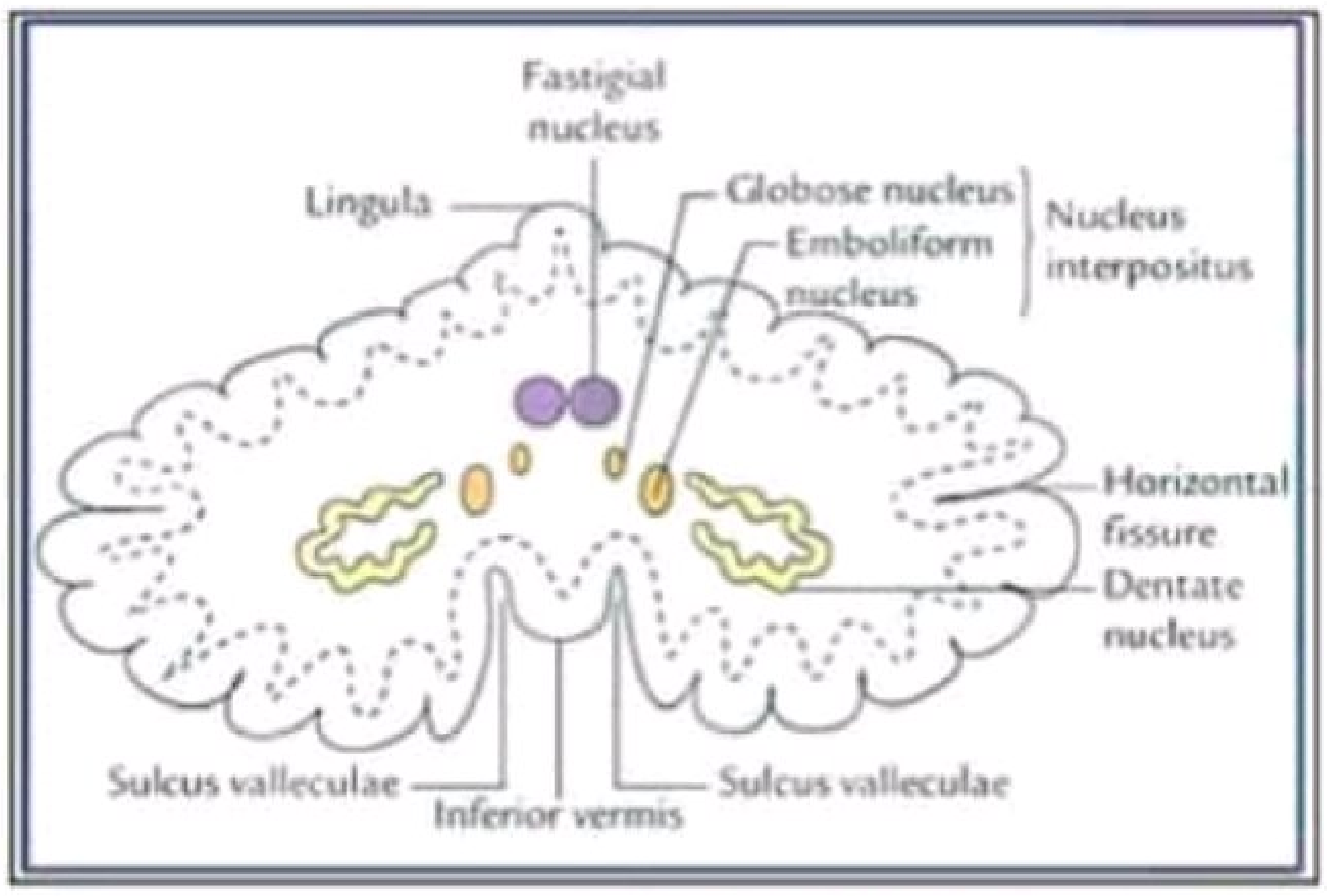
ANATOMY OF CEREBELLUM

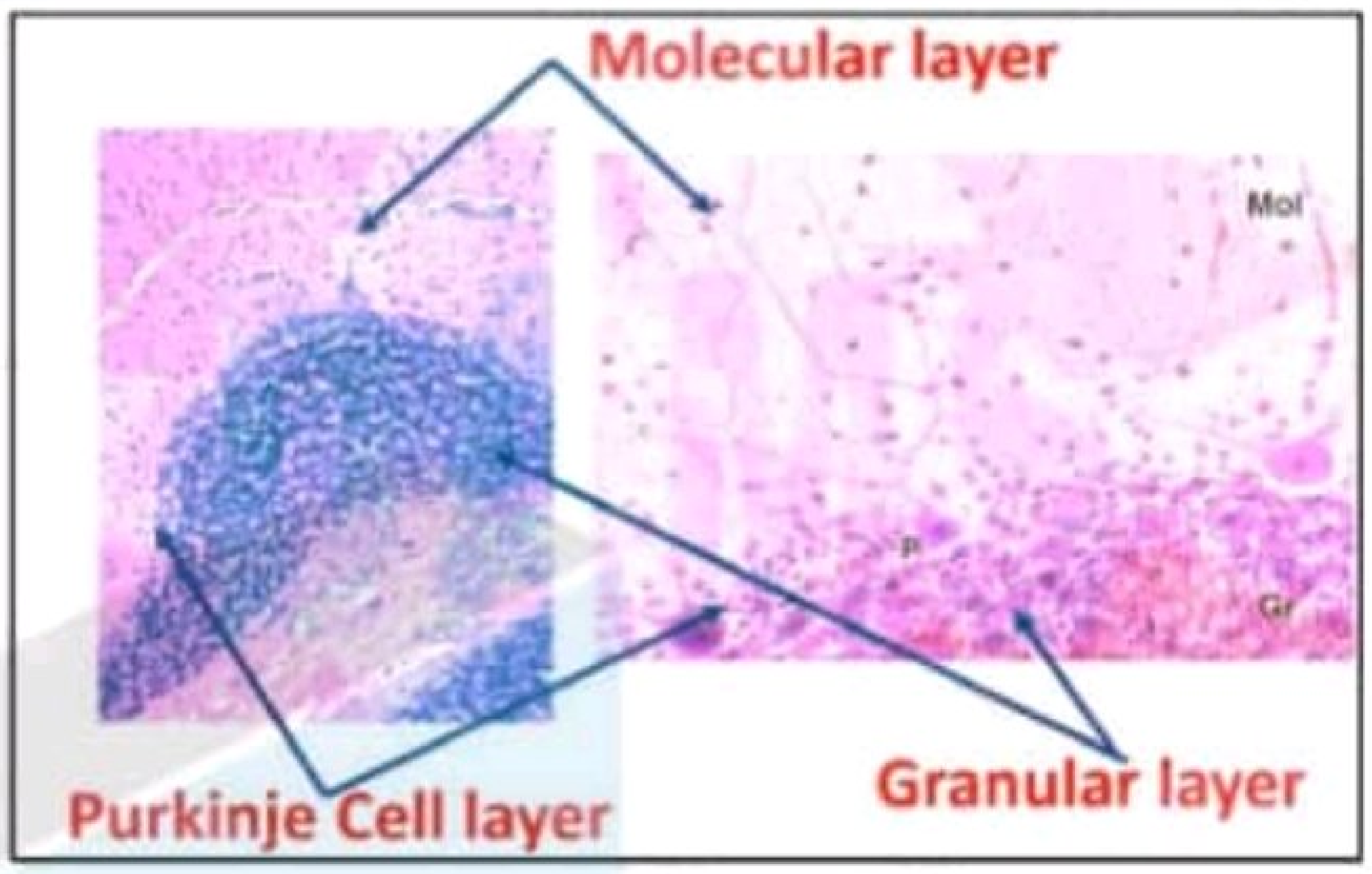

Superior surface
Anterior cerebellar notch
Superior vermis
Central lobule (II and III)
Culmen (IV and V)
Declive (VI)
Folium (VIIA)
Posterior cerebellar notch
Anterior lobe
Quadrangular lobule (H IV and V)
Primary fissure
Horizontal fissure
Simple lobule (H VI)
Posterior lobe
Postlunate fissure
Superior semilunar (ansiform) lobule (H VIIA)
Horizontal fissure
Inferior semilunar (caudal) lobule (H VIIB)

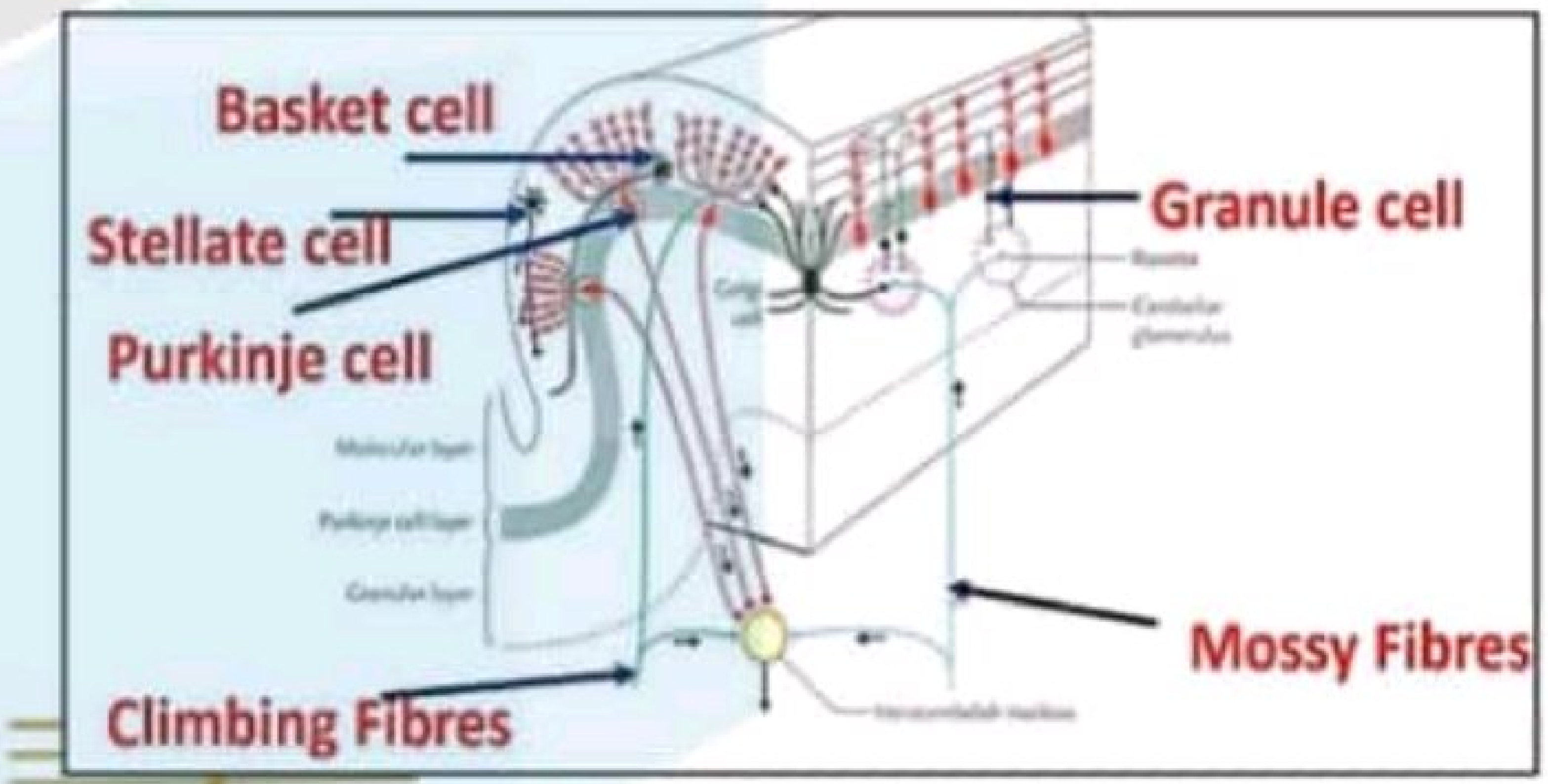

Inferior surface
Superior vermis
Central lobule
Lingula (I)
Superior medullary velum
Flocculus (H X)
4th ventricle
Inferior medullary velum
Inferior vermis
Nodule (X)
Uvula (IX)
Pyramid (VIII)
Tuber (VIIB)
Posterior cerebellar notch
Anterior lobe
Wing of central lobule
Superior
Middle
Inferior
Cerebellar peduncles
Flocculonodular lobe
Posterolateral (dorsolateral) fissure
Retrotonsillar fissure
Posterior lobe
Tonsil
Biventer lobule (H VIII)
Secondary (postpyramidal) fissure
Horizontal fissure
Inferior semilunar (caudal) lobule (H VIIB)

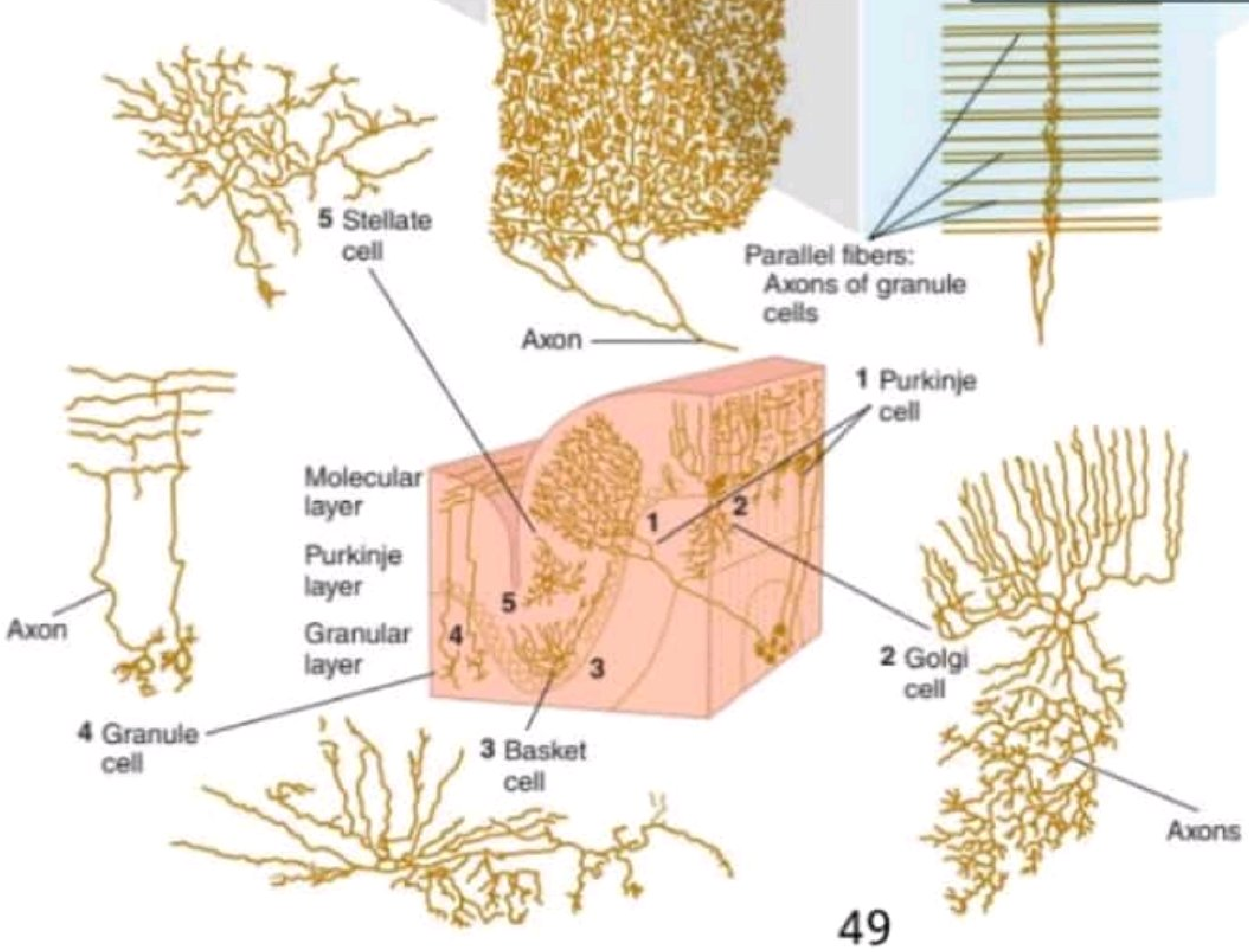

Decussation of superior cerebellar peduncles
4th ventricle
Superior medullary velum
Cerebellar nuclei
Fastigial
Globose
Dentate
Emboliform
Cerebral crus
Medial longitudinal fasciculus
Superior cerebellar peduncle
Lingula (I)
Vermis

Section in plane of superior cerebellar peduncle

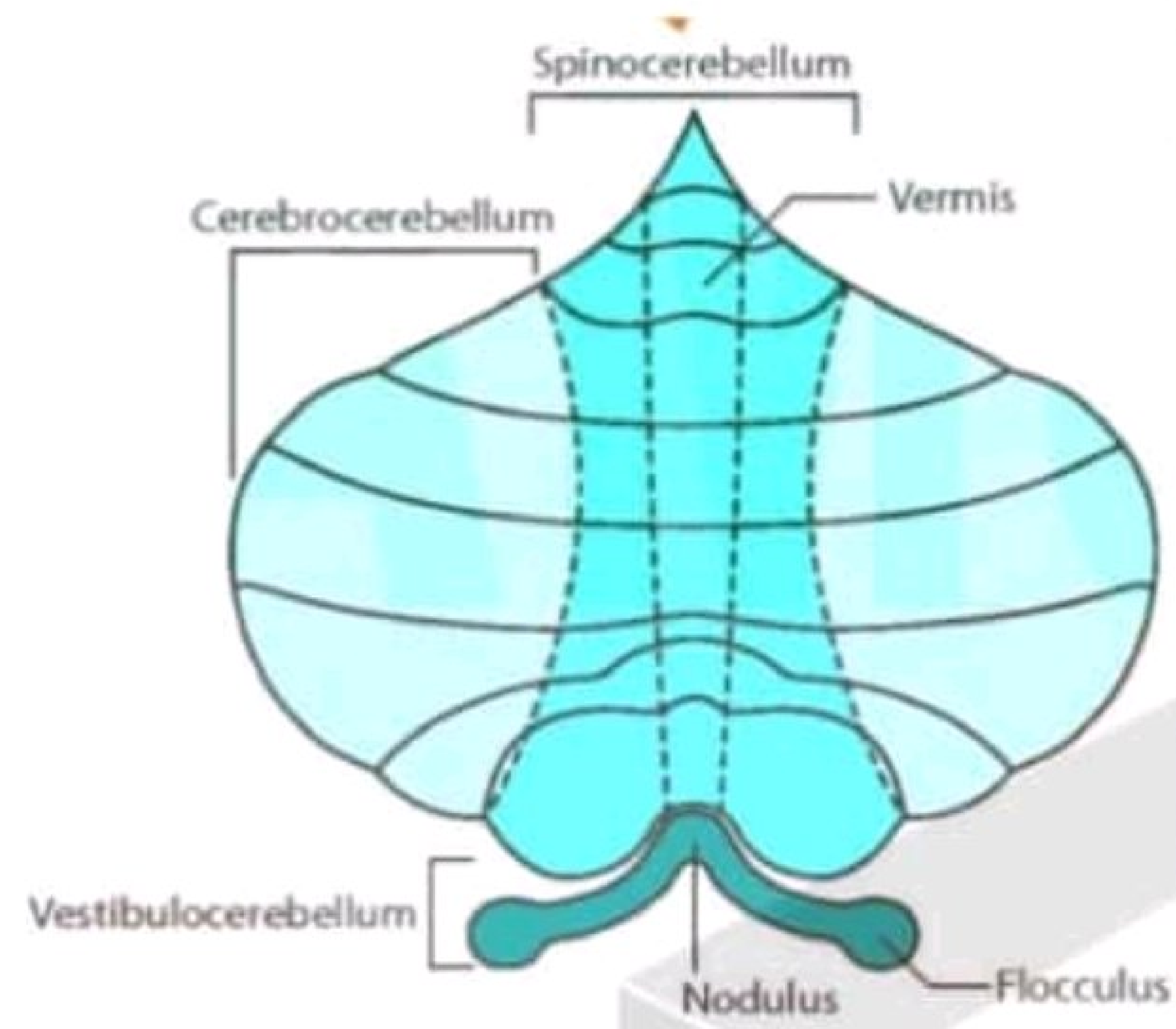

Fastigial nucleus
Lingula
Globose nucleus
Emboliform nucleus
Nucleus interpositus
Horizontal fissure
Dentate nucleus
Sulcus valleculae
Inferior vermis
Sulcus valleculae

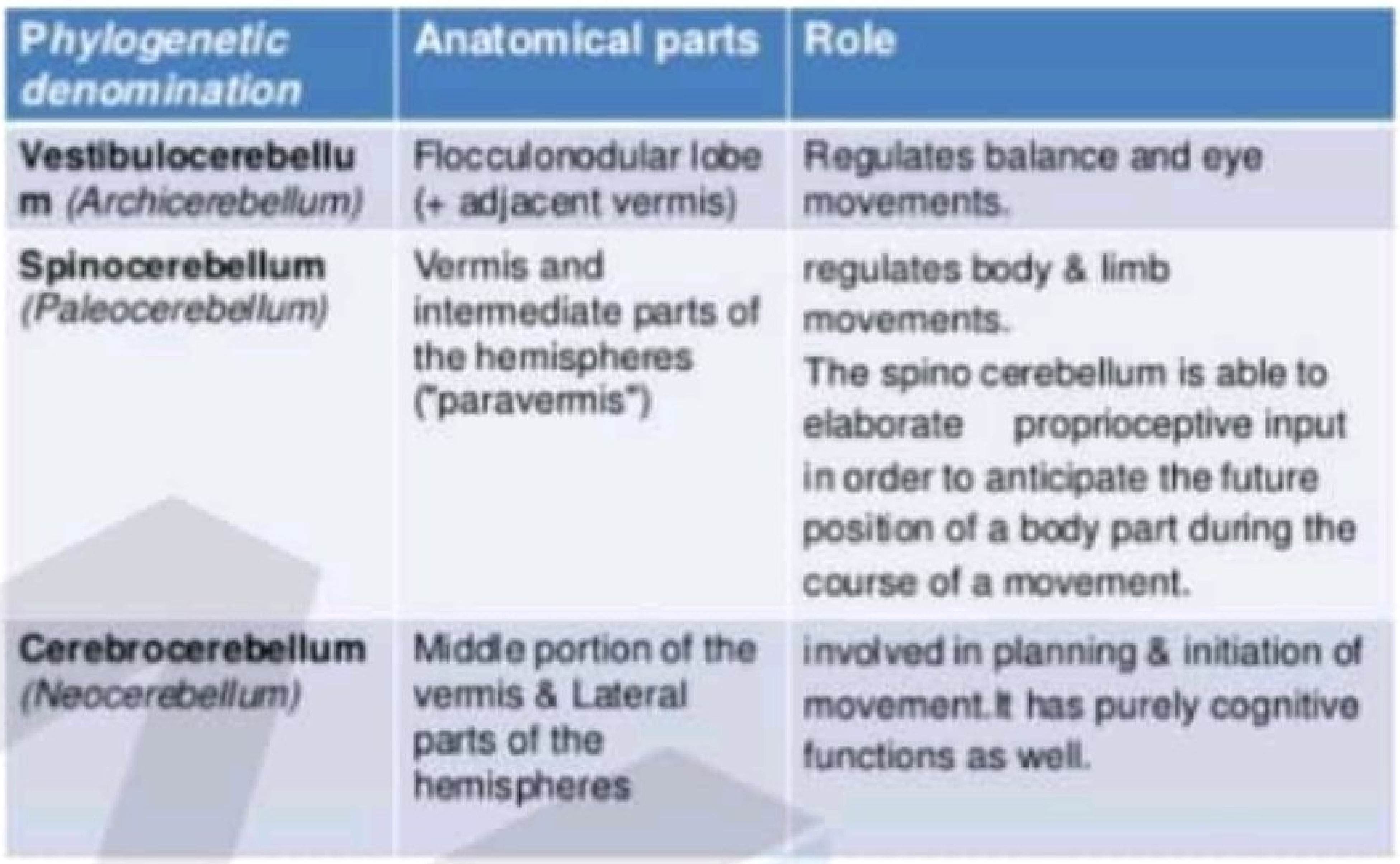

Molecular layer
Mol
P
Gr
Purkinje Cell layer
Granular layer


Basket cell
Stellate cell
Purkinje cell
Granule cell
Golgi cell
Molecular layer
Purkinje cell layer
Granular layer
Mossy Fibres
Climbing Fibres


5 Stellate cell
Parallel fibers: Axons of granule cells
Axon
1 Purkinje cell
Molecular layer
Purkinje layer
Granular layer
1
2
5
4
3
2 Golgi cell
Axon
4 Granule cell
3 Basket cell
Axons

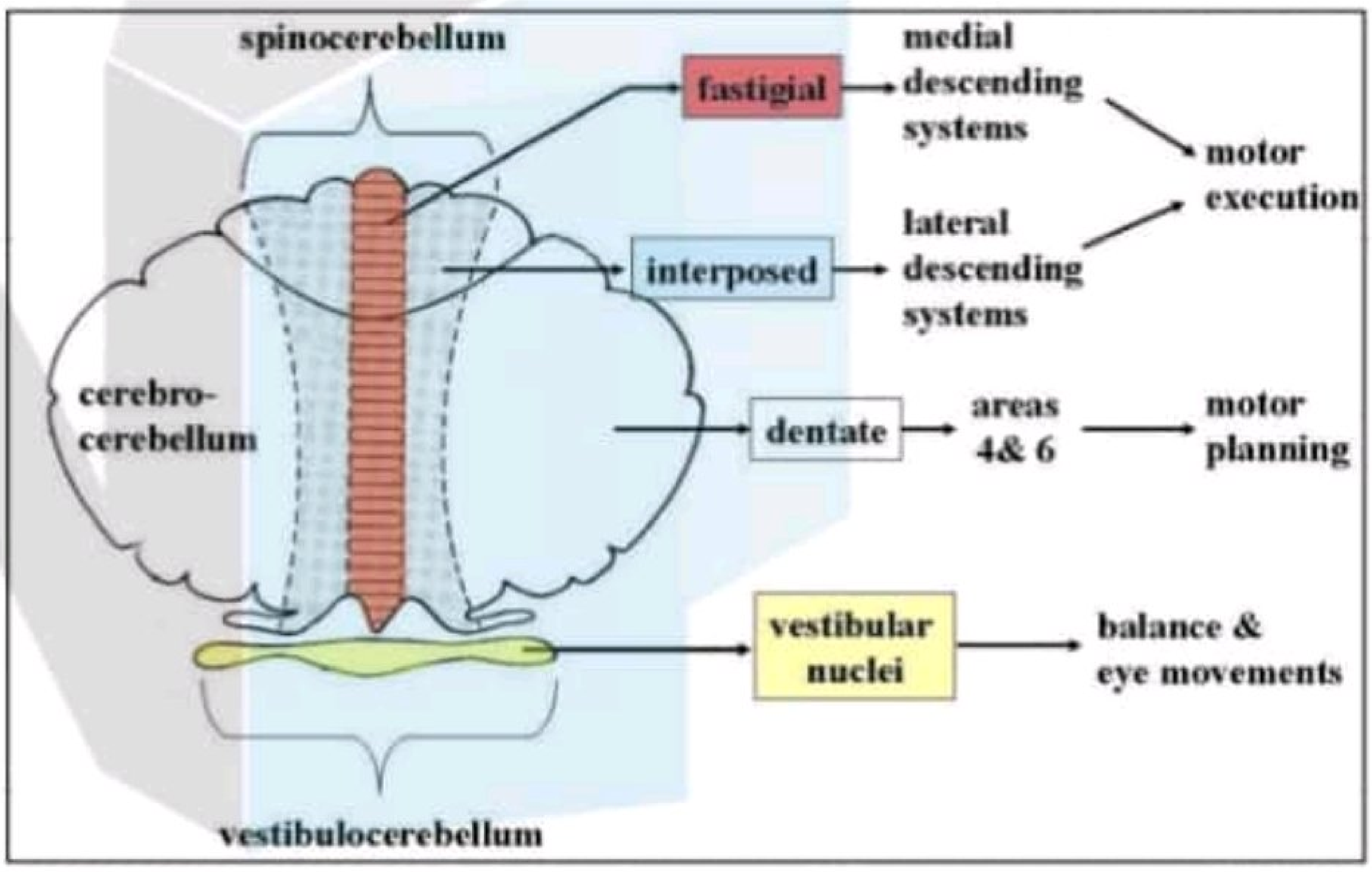
PHYSIOLOGY


Spinocerebellum
Cerebrocerebellum
Vermis
Vestibulocerebellum
Nodulus
Flocculus



Phylogenetic denomination	Anatomical parts	Role
Vestibulocerebellum *(Archicerebellum)*	Flocculonodular lobe (+ adjacent vermis)	Regulates balance and eye movements.
Spinocerebellum *(Paleocerebellum)*	Vermis and intermediate parts of the hemispheres ("paravermis")	regulates body & limb movements. The spino cerebellum is able to elaborate proprioceptive input in order to anticipate the future position of a body part during the course of a movement.
Cerebrocerebellum *(Neocerebellum)*	Middle portion of the vermis & Lateral parts of the hemispheres	involved in planning & initiation of movement.It has purely cognitive functions as well.

- **Spinocerebellum**; Medial part → Proximal muscles, Lateral part → Distal muscles
- **Flocculonodular** lobe has no nuclei, but has direct contact with the vestibular system
- **Medial spinocerebellum** has fastigial nuclei are is responsible for axial skeleton muscles
- **Lateral spinocerebellum** has Interposed nucleus (Globus + Emboliform) are is responsible for distal skeleton muscles


spinocerebellum
fastigial
medial descending systems
motor execution
interposed
lateral descending systems
cerebro-cerebellum
dentate
areas 4& 6
motor planning
vestibular nuclei
balance & eye movements
vestibulocerebellum

Output of
- Cerebellar cortex is from the Purkinje cells
- Cerebellum is from the Deep Nuclei (Excitatory)

Purkinje fibres project to deep nuclei and inhibit their excitatory impulse

Cells of the cerebellum

- Stellate cells
- Basket cells

External molecular layer

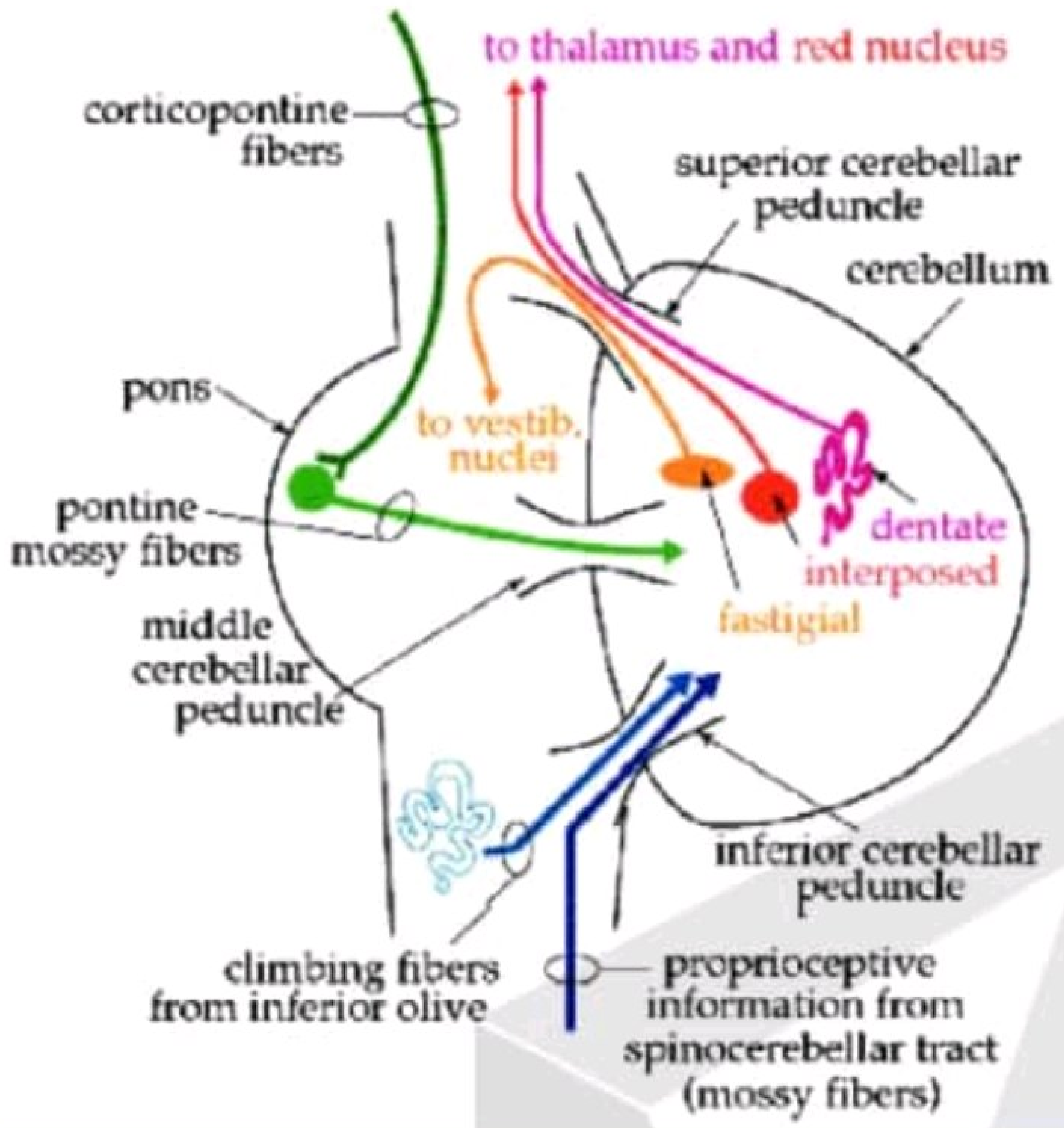
- Purkinje cells
- Granule cells
- Golgi cells

(Only excitatory cell is the GRANULE CELL)
Inner granular layer

Input is via
- Climbing fibres
- Mossy fibres

Input is of **proprioception** from the whole body

Climbing fibres- Strong Excitatory impulse
Mossy fibres- Weak Excitatory impulse


to thalamus and red nucleus
corticopontine fibers
superior cerebellar peduncle
cerebellum
pons
to vestib. nuclei
pontine mossy fibers
dentate
interposed
fastigial
middle cerebellar peduncle
inferior cerebellar peduncle
climbing fibers from inferior olive
proprioceptive information from spinocerebellar tract (mossy fibers)

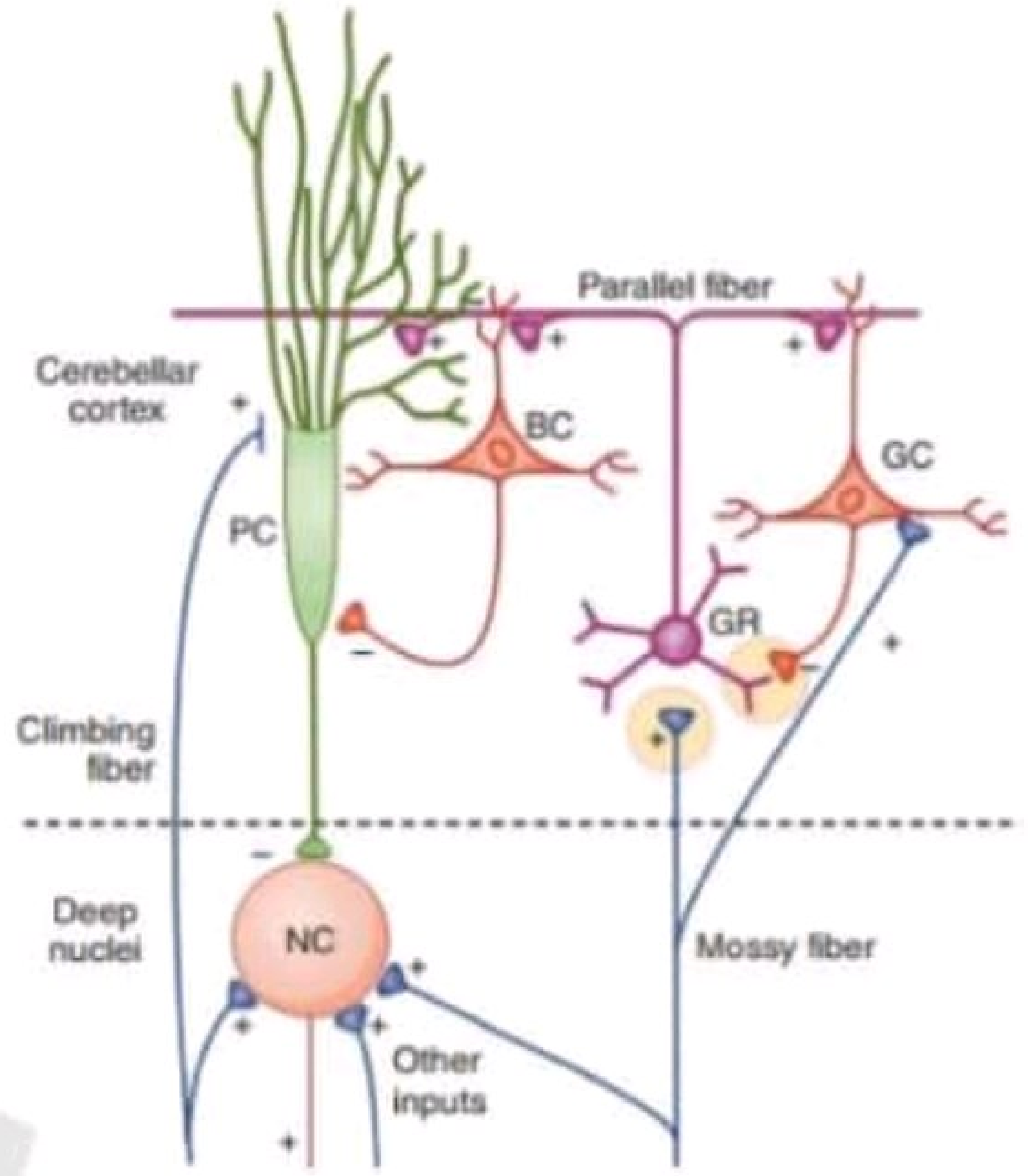
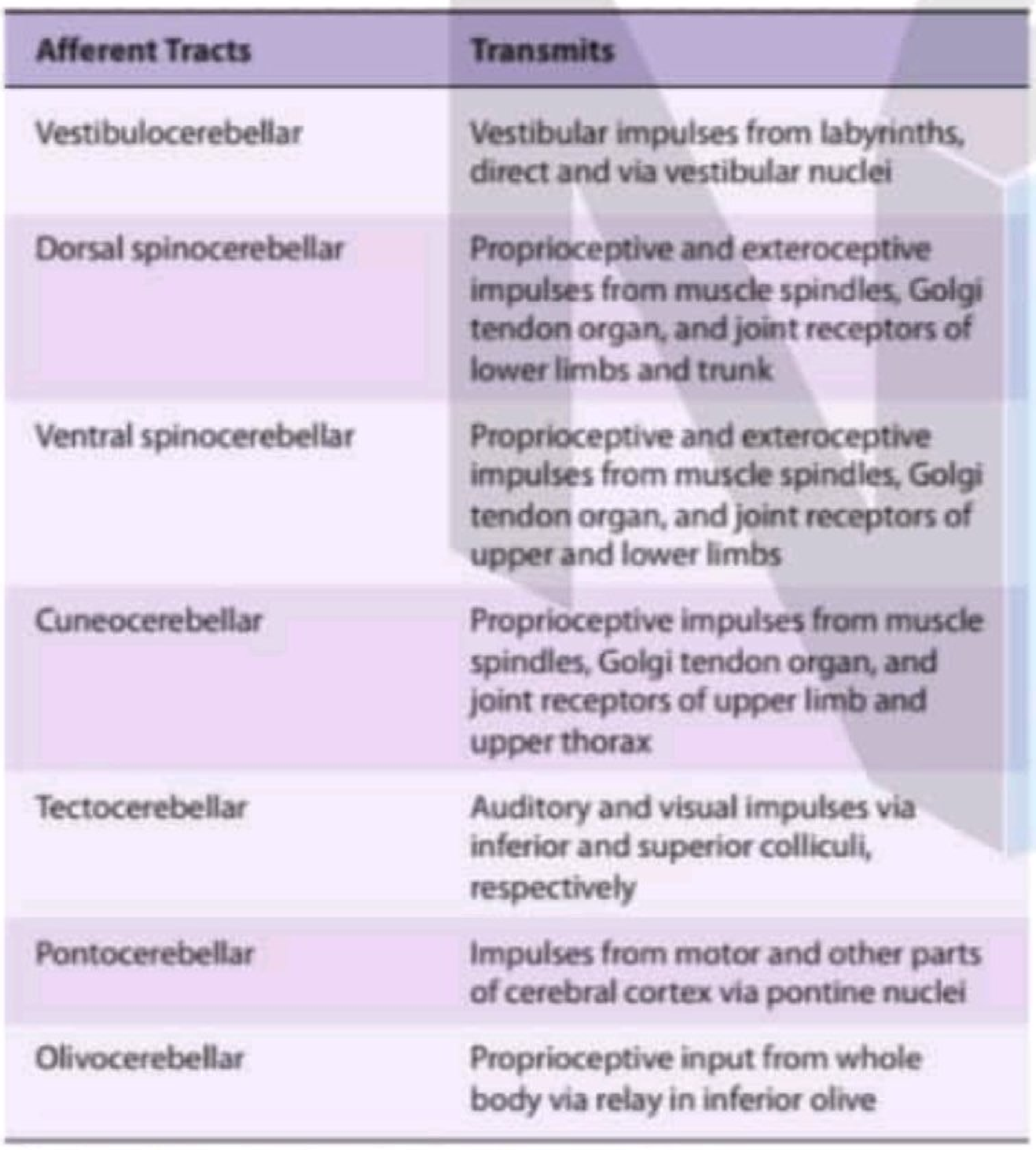

Parallel fiber
Cerebellar cortex
BC
GC
PC
GR
Climbing fiber
Deep nuclei
NC
Mossy fiber
Other inputs
+
−

FIGURE 12–18 Diagram of neural connections in the cerebellum. Plus (+) and minus (–) signs indicate whether endings are excitatory or inhibitory. BC, basket cell; GC, Golgi cell; GR, granule cell; NC, cell in deep nucleus; PC, Purkinje cell. Note that PCs and BCs are inhibitory. The connections of the stellate cells, which are not shown, are similar to those of the basket cells, except that they end for the most part on Purkinje cell dendrites.



Afferent Tracts	Transmits
Vestibulocerebellar	Vestibular impulses from labyrinths, direct and via vestibular nuclei
Dorsal spinocerebellar	Proprioceptive and exteroceptive impulses from muscle spindles, Golgi tendon organ, and joint receptors of lower limbs and trunk
Ventral spinocerebellar	Proprioceptive and exteroceptive impulses from muscle spindles, Golgi tendon organ, and joint receptors of upper and lower limbs
Cuneocerebellar	Proprioceptive impulses from muscle spindles, Golgi tendon organ, and joint receptors of upper limb and upper thorax
Tectocerebellar	Auditory and visual impulses via inferior and superior colliculi, respectively
Pontocerebellar	Impulses from motor and other parts of cerebral cortex via pontine nuclei
Olivocerebellar	Proprioceptive input from whole body via relay in inferior olive

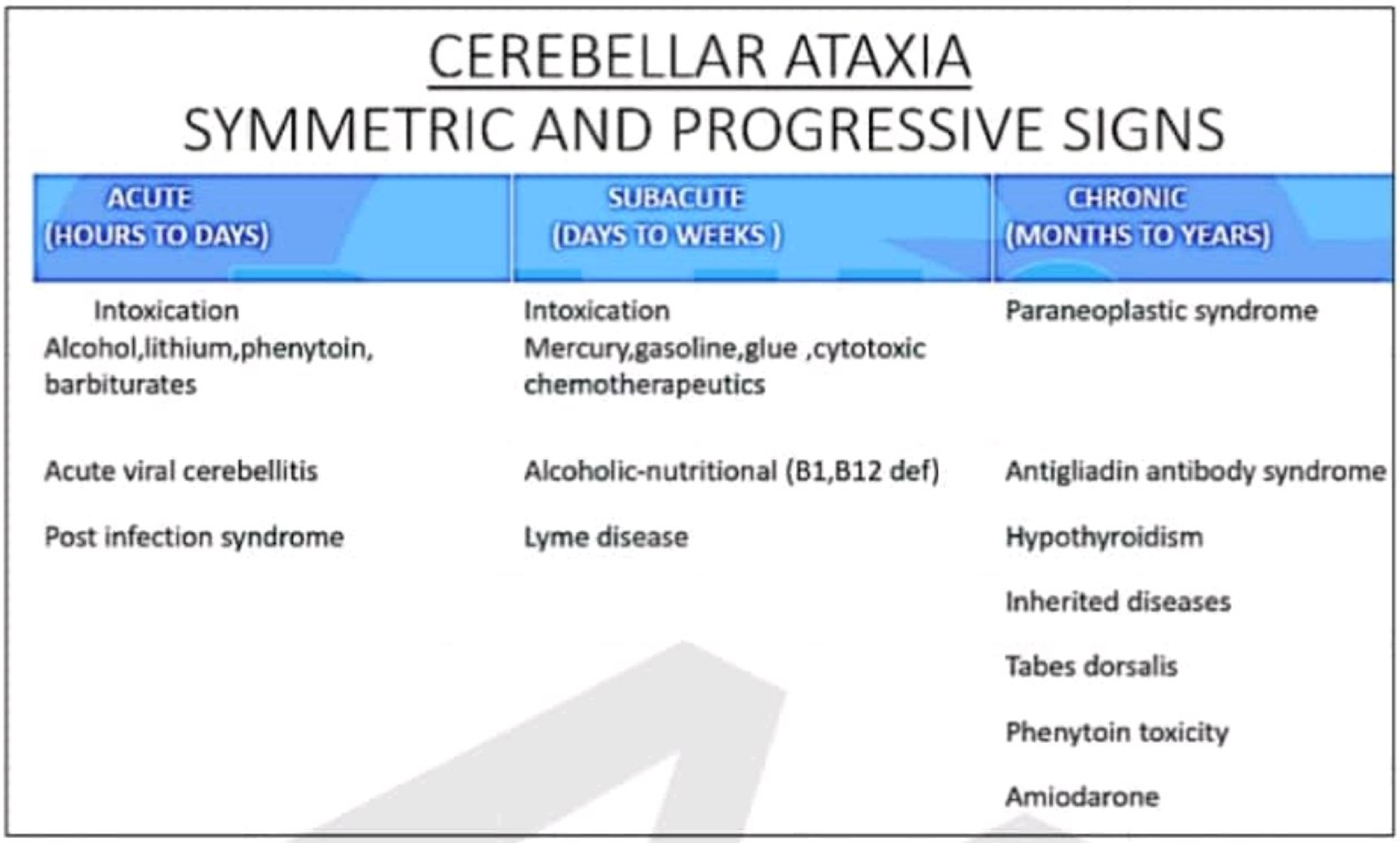
The climbing fibre stimulates the purkinje's cell in the beginning of the movement which then exerts an inhibtory impulse on the Deep Nuclei cell and controls the overdo of the movement

In the lesion of the cerebellar cortex, this inhibtion of the PC is lost, henceforth leding to clinical signs like:

- Past pointing
- Overshoot
- Rebound phenomenon
- Intentional tremor
- Dysdiadochokinesia
- Failed Heel Shin test
- Pendular knee jerk
- Failed Finger nose test

The basket and stellate cells are also excited by granule cells via their parallel fibers; and the basket and stellate cells, in turn, inhibit the Purkinje cells **(feedforward inhibition)**. Golgi cells are excited by the mossy fibre collaterals and parallel fibers, and they inhibit transmission from mossy fibers to granule cells **(feedback inhibition)**.

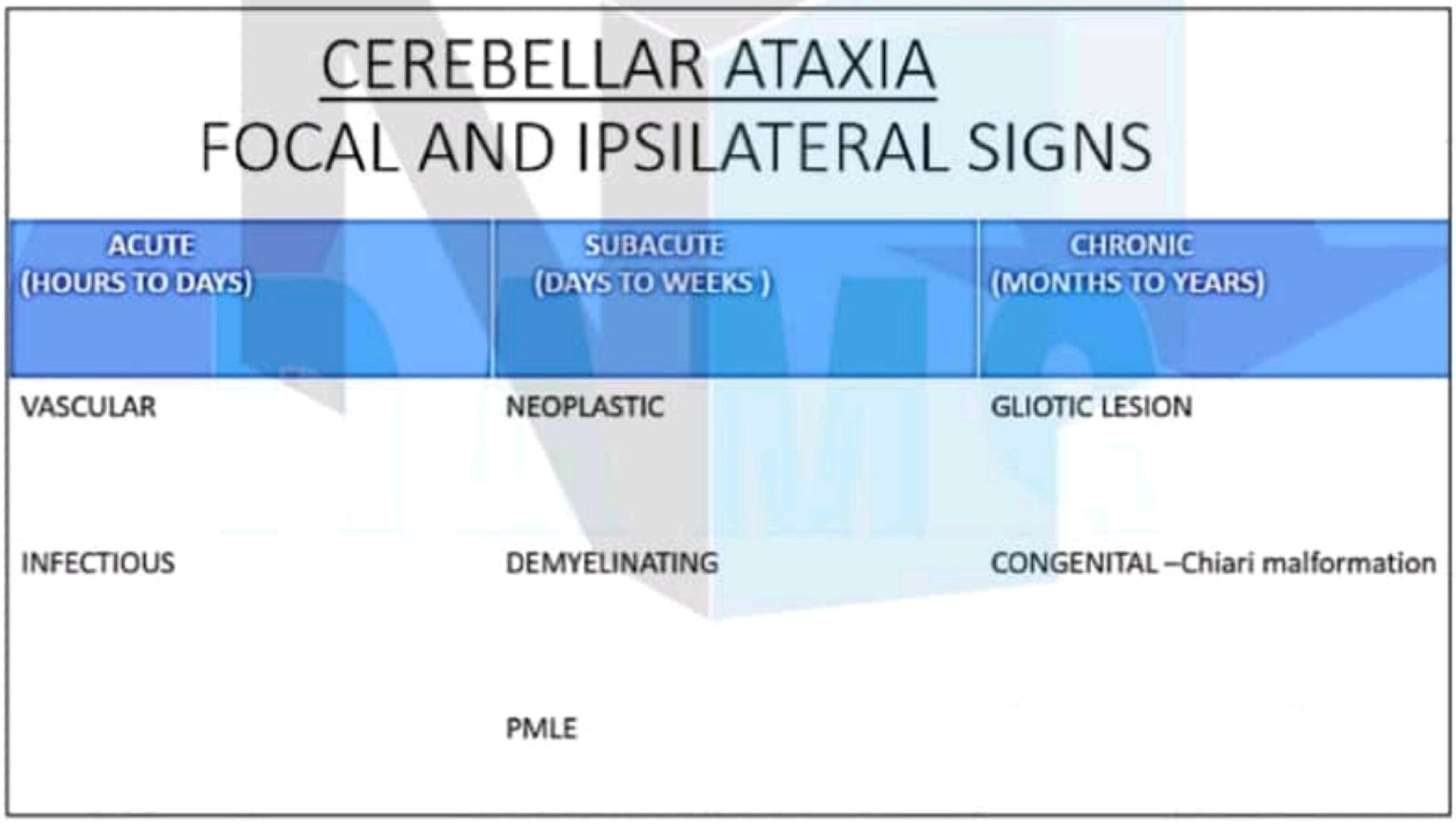
The neurotransmitter released by the stellate, basket, Golgi, and Purkinje cells is GABA, whereas the granule cells release glutamate. GABA acts via GABA A receptors, but the combinations of subunits in these receptors vary from one cell type to the next. The granule cell is unique in that it appears to be the only type of neuron in the CNS that has a GABA A receptor containing the α6 subunit.



CEREBELLAR ATAXIA
SYMMETRIC AND PROGRESSIVE SIGNS

ACUTE (HOURS TO DAYS)	SUBACUTE (DAYS TO WEEKS)	CHRONIC (MONTHS TO YEARS)
Intoxication Alcohol,lithium,phenytoin, barbiturates	Intoxication Mercury,gasoline,glue ,cytotoxic chemotherapeutics	Paraneoplastic syndrome
Acute viral cerebellitis	Alcoholic-nutritional (B1,B12 def)	Antigliadin antibody syndrome
Post infection syndrome	Lyme disease	Hypothyroidism
		Inherited diseases
		Tabes dorsalis
		Phenytoin toxicity
		Amiodarone

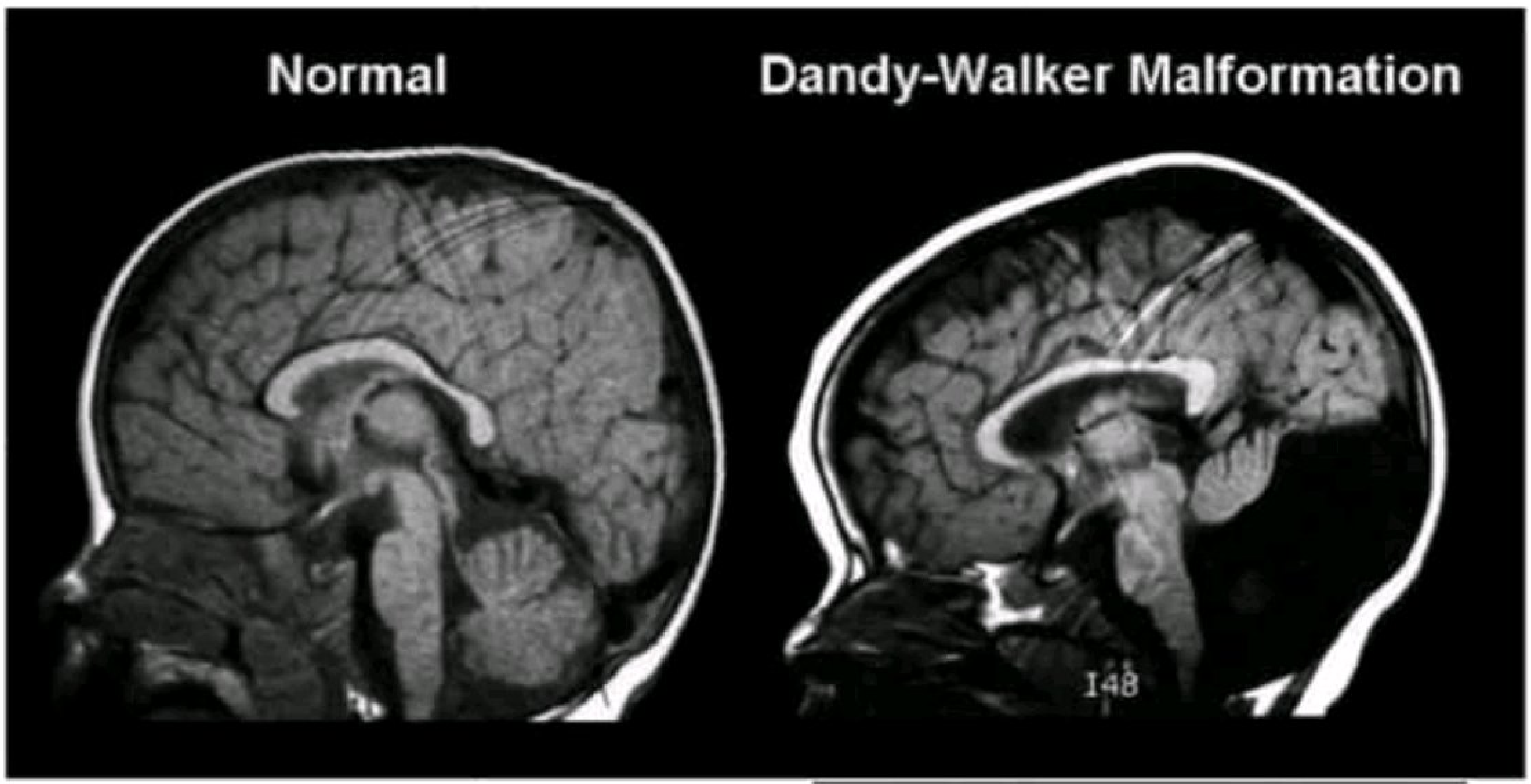
- PHENYTOIN intoxication can be both Acute or Chronic Ataxia
- Phenytoin and Tabes Dorsalis- are examples of Symmetrical Ataxia



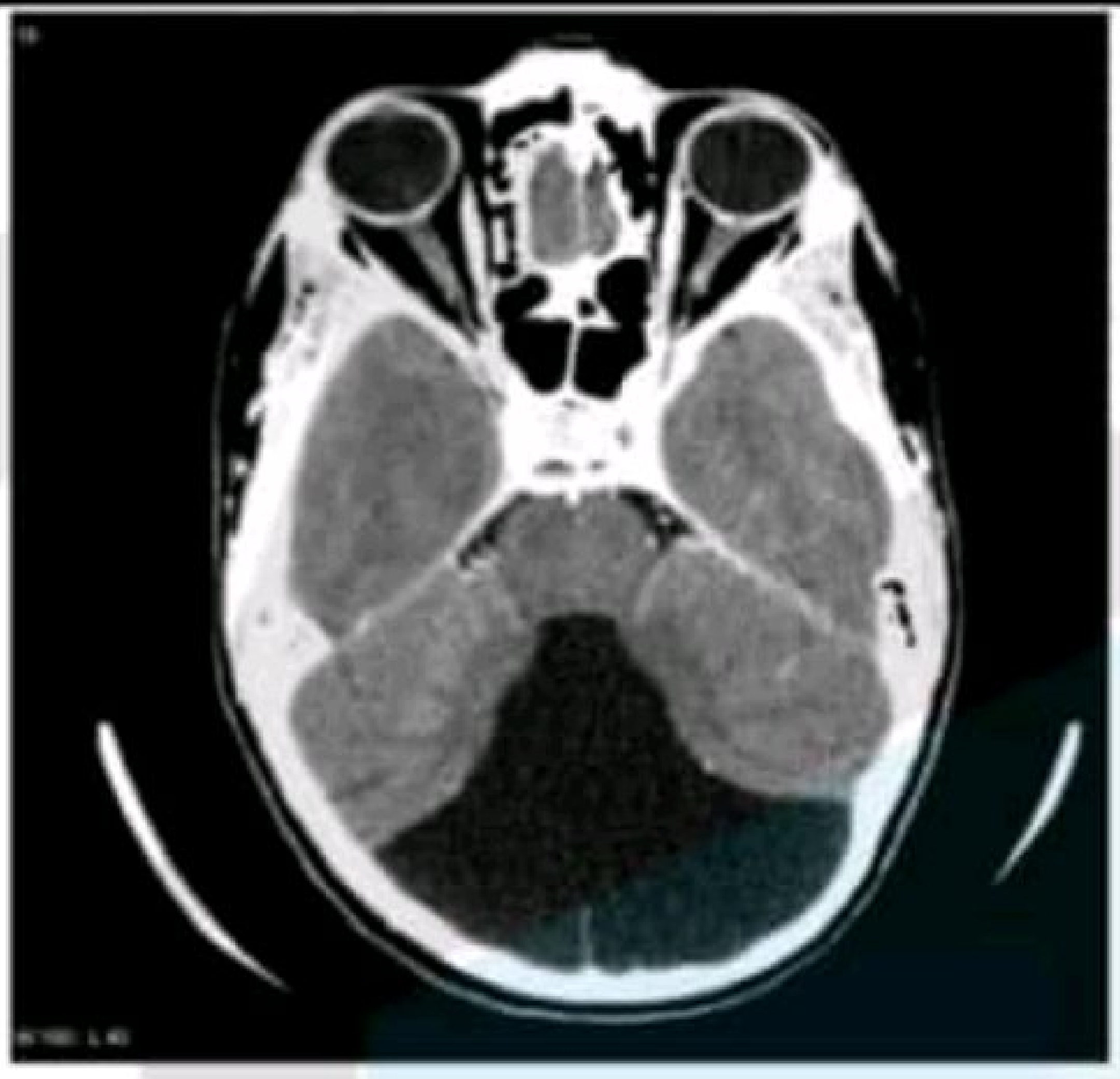
CEREBELLAR ATAXIA
FOCAL AND IPSILATERAL SIGNS

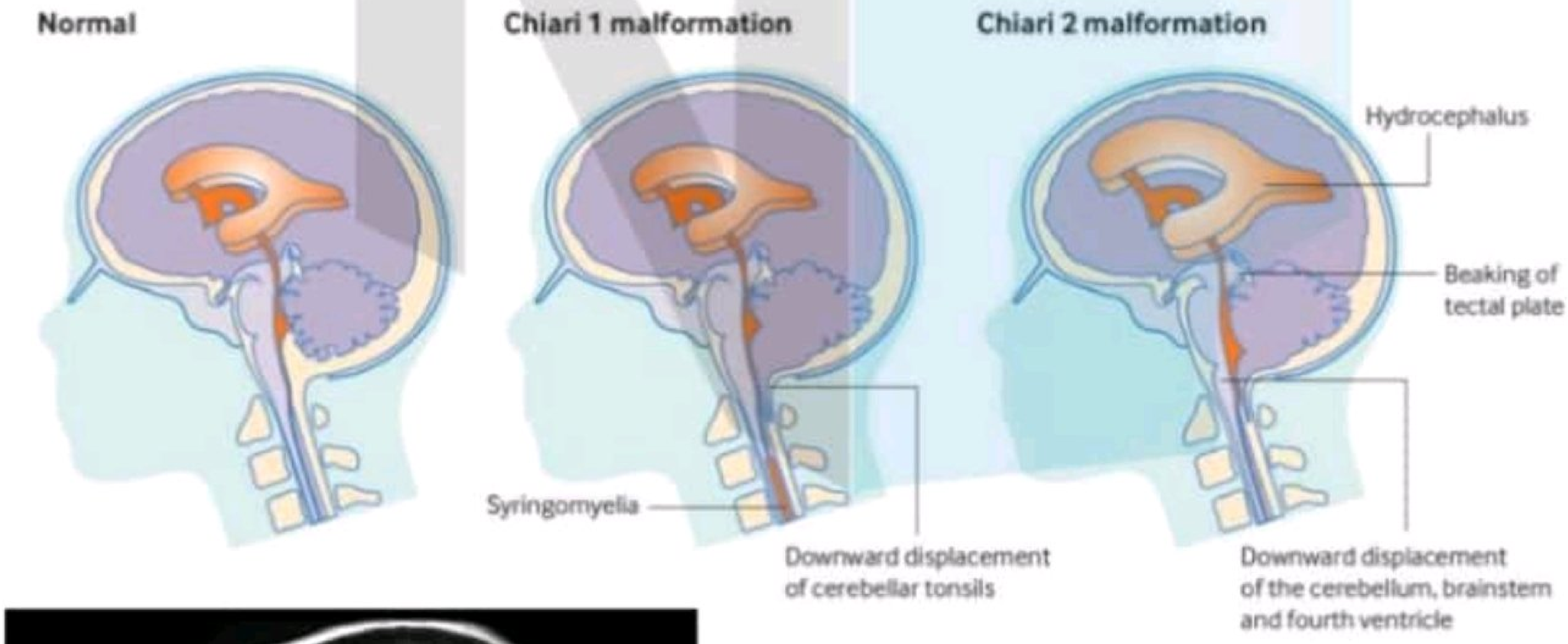
ACUTE (HOURS TO DAYS)	SUBACUTE (DAYS TO WEEKS)	CHRONIC (MONTHS TO YEARS)
VASCULAR	NEOPLASTIC	GLIOTIC LESION
INFECTIOUS	DEMYELINATING	CONGENITAL –Chiari malformation
	PMLE	

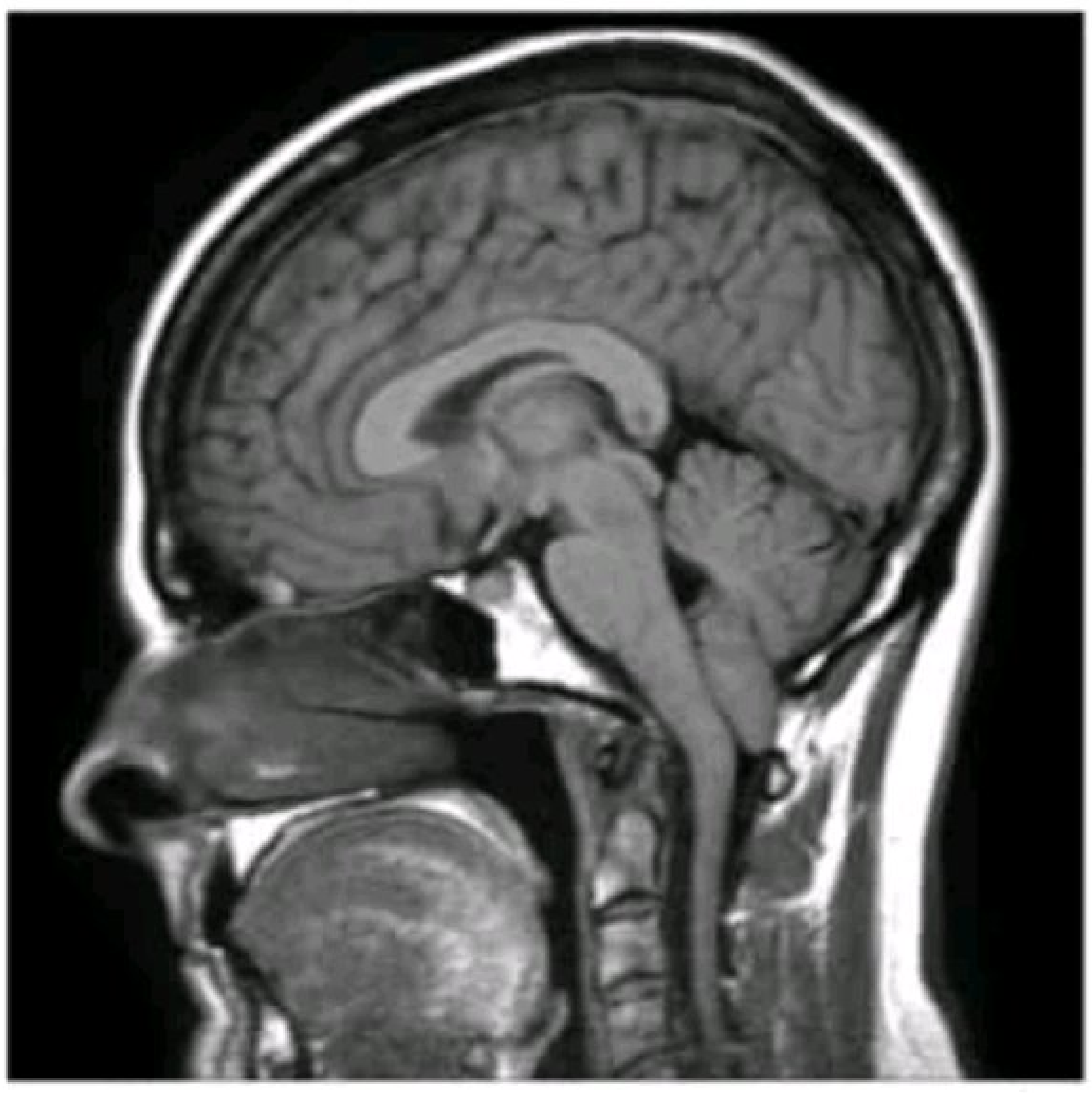
PMLE- Progressive Multifocal LeukoEncephalopathy


Normal
Dandy-Walker Malformation
I48

DANDY WALKER
Is associated with
Vermis Agenesis




Normal
Chiari 1 malformation
Chiari 2 malformation
Hydrocephalus
Beaking of tectal plate
Syringomyelia
Downward displacement of cerebellar tonsils
Downward displacement of the cerebellum, brainstem and fourth ventricle



CHIARI TYPE 1
Showing Tonsillar hernia

MULTIPLE SCLEROSIS

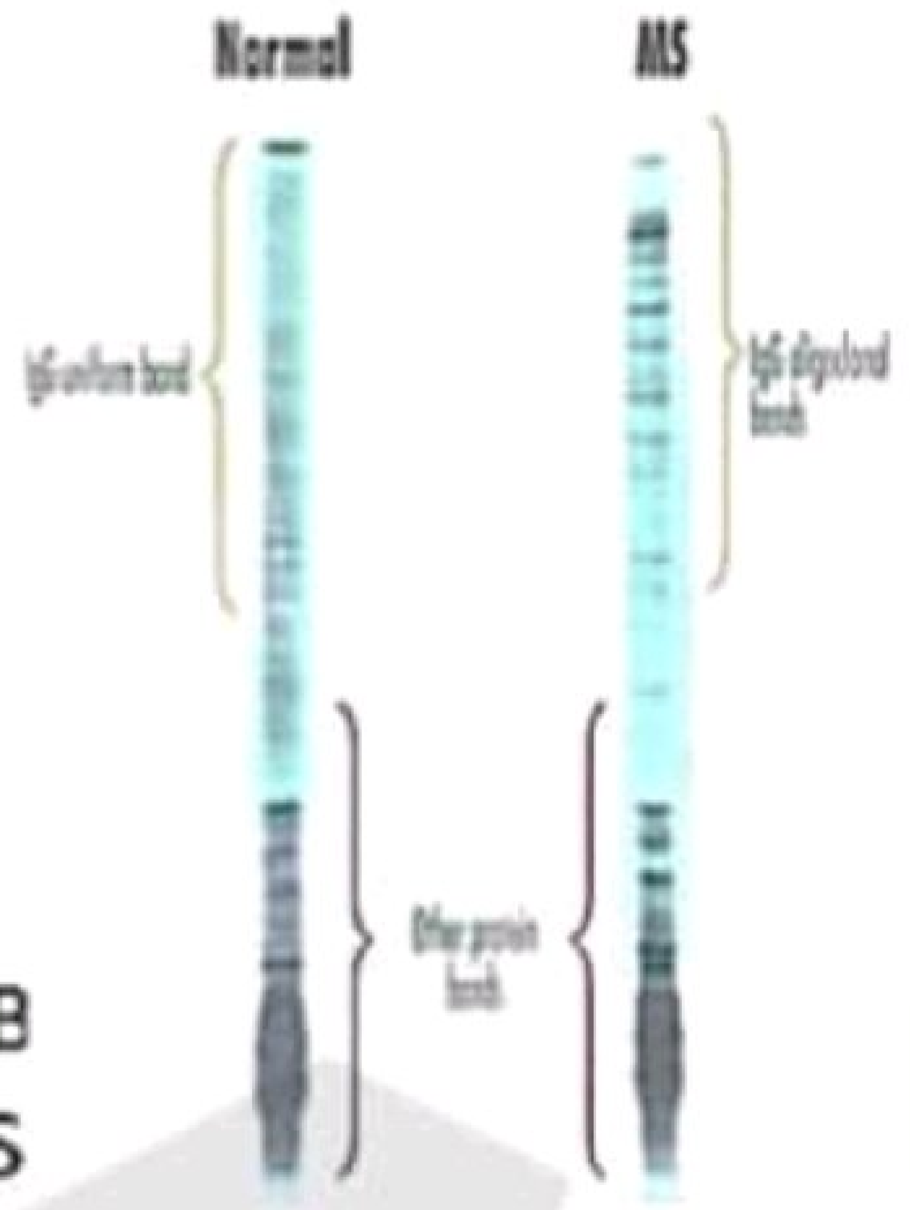
Types:

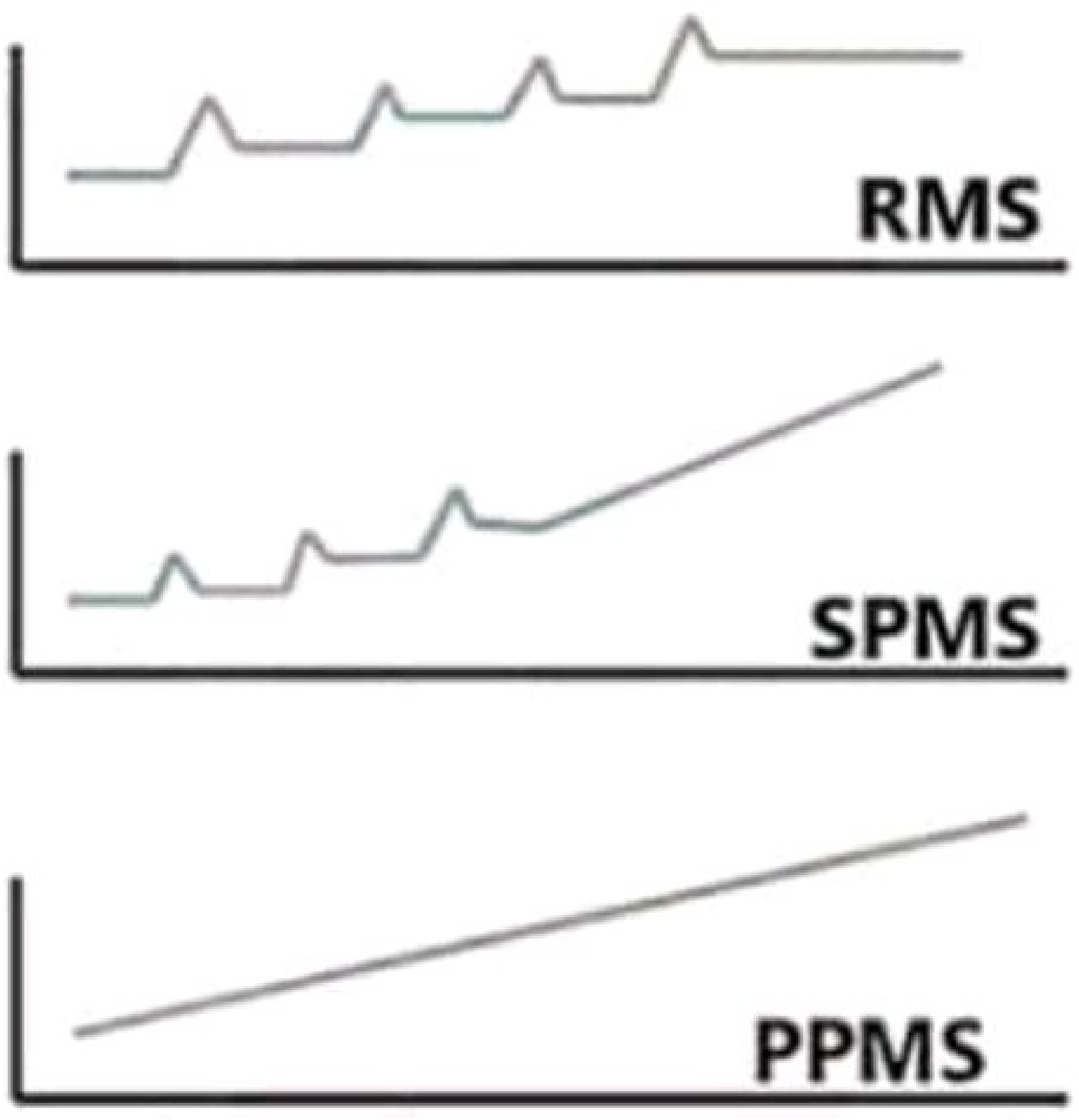
1. Relapsing MS (90%)
2. Primary progressive MS (10%)
3. Secondary Progressive MS (about 2% risk)

- **Earliest symptom**
  Sensory loss
- **M.C symptom**
  Weakness

Diagnostic criteria
Mac Donald Criteria

Oligoclonal Bands(OCB
>2 seen in >75% of MS



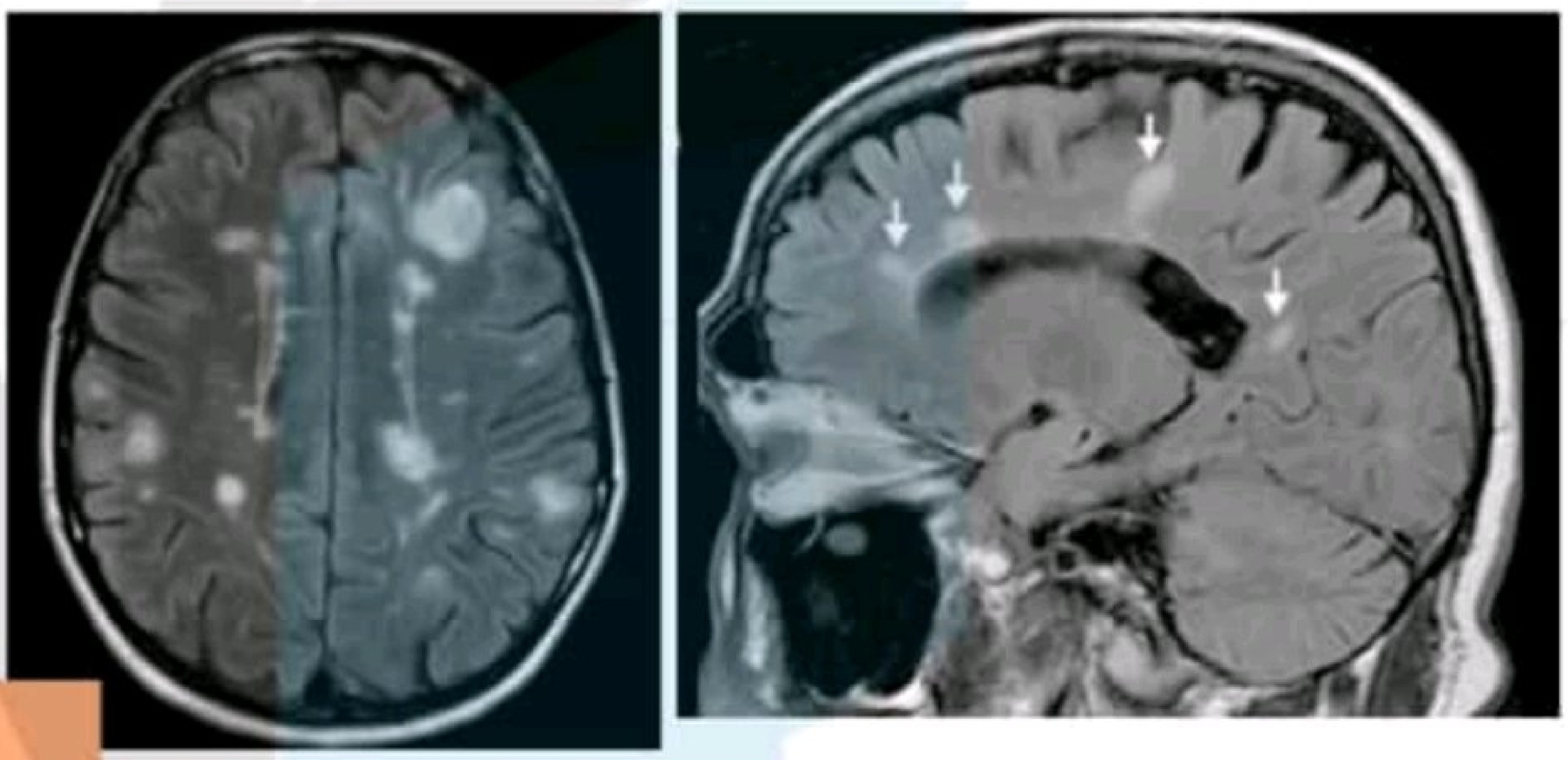


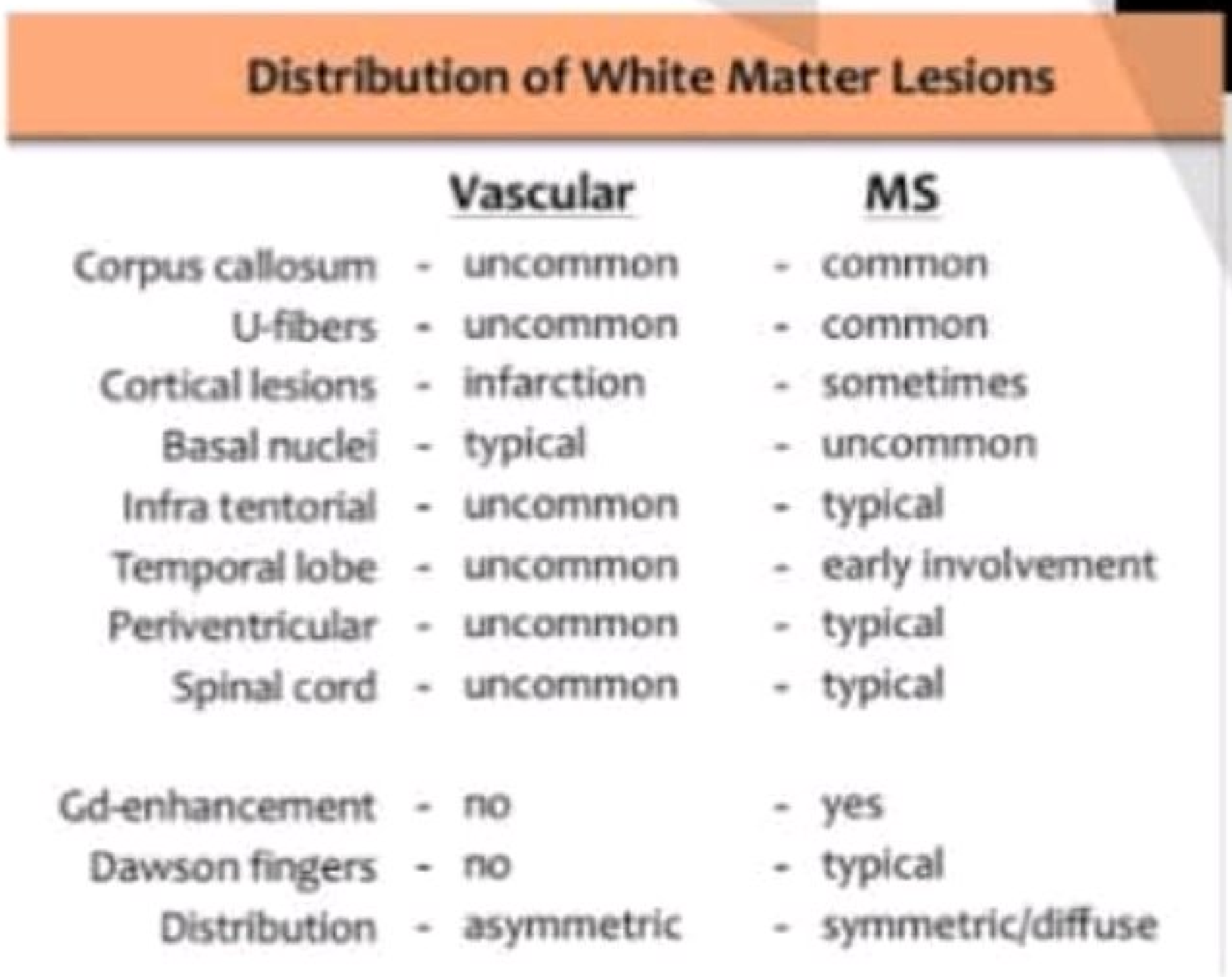
Dx: Agarose Gel Electrophoresis

RADIOLOGY

MRI: Subcortical Periventricular plaques in the white matter

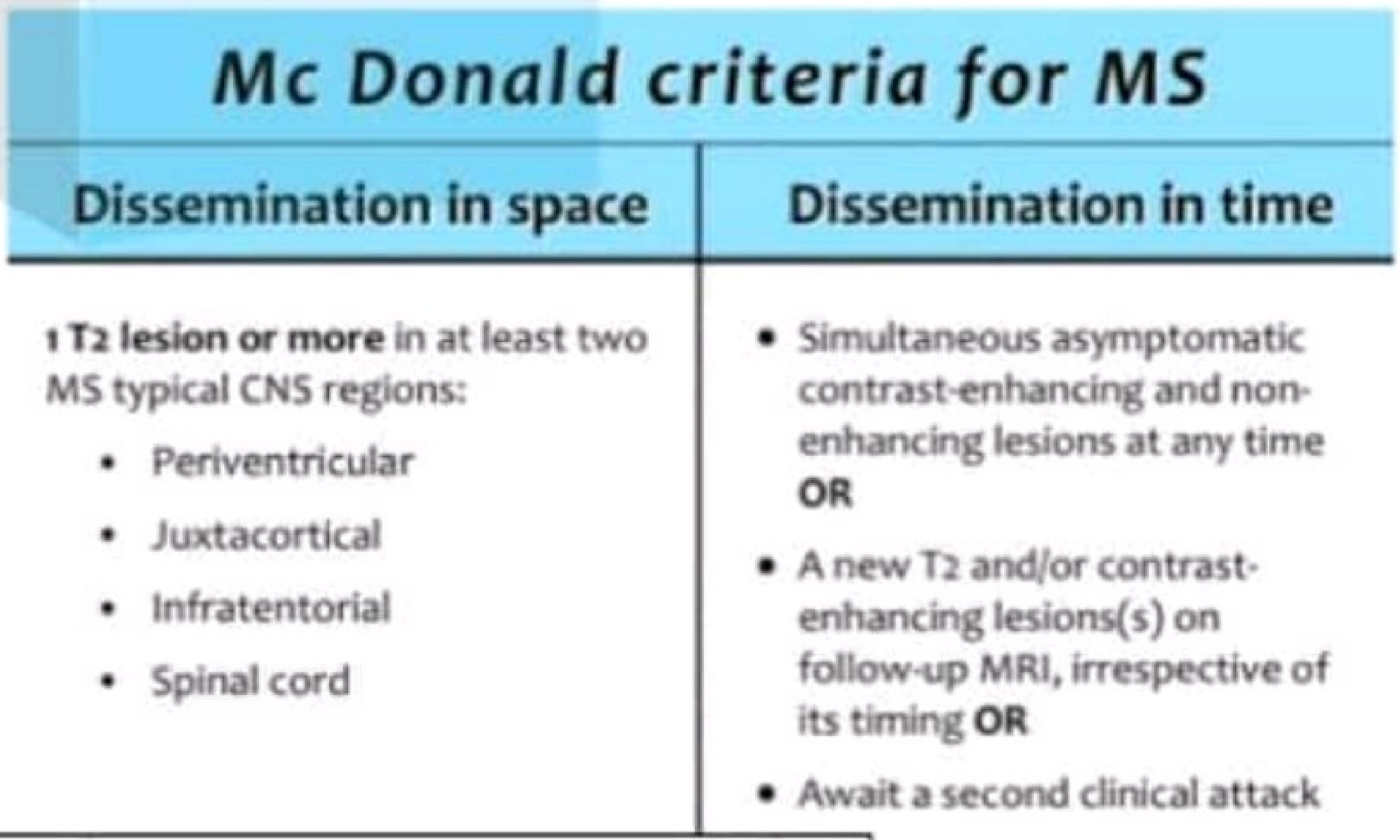
Sagittal Section: Perivenular plaques known as **DAWSON'S FINGERS**





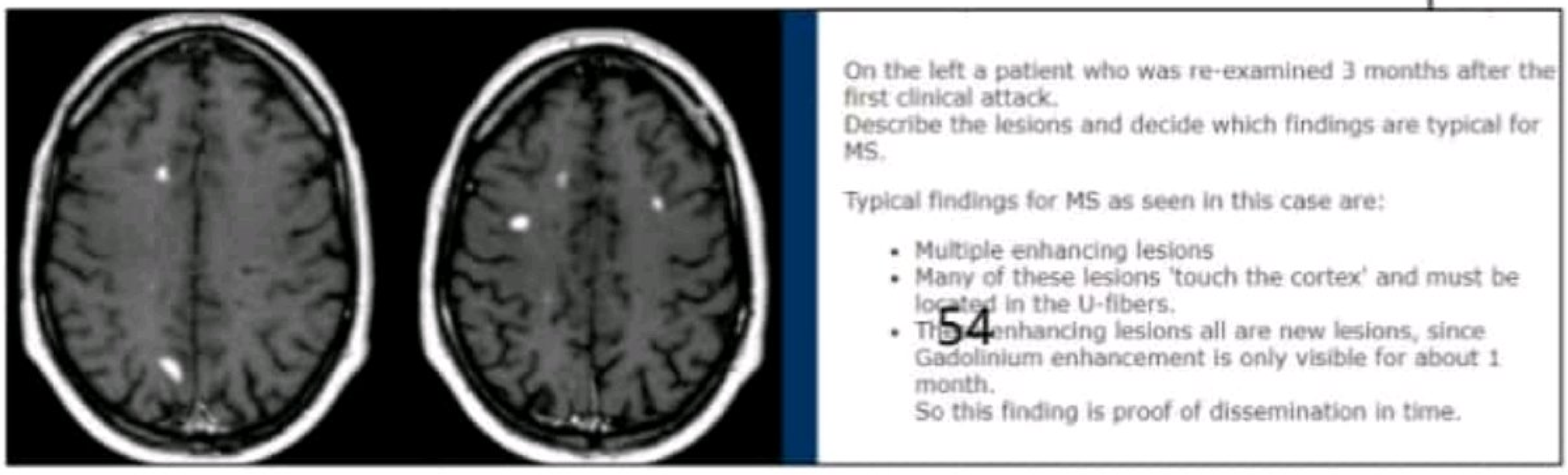
Distribution of White Matter Lesions

	Vascular	MS
Corpus callosum	- uncommon	- common
U-fibers	- uncommon	- common
Cortical lesions	- infarction	- sometimes
Basal nuclei	- typical	- uncommon
Infra tentorial	- uncommon	- typical
Temporal lobe	- uncommon	- early involvement
Periventricular	- uncommon	- typical
Spinal cord	- uncommon	- typical
Gd-enhancement	- no	- yes
Dawson fingers	- no	- typical
Distribution	- asymmetric	- symmetric/diffuse



Mc Donald criteria for MS

Dissemination in space	Dissemination in time
1 T2 lesion or more in at least two MS typical CNS regions: • Periventricular • Juxtacortical • Infratentorial • Spinal cord	• Simultaneous asymptomatic contrast-enhancing and non-enhancing lesions at any time **OR** • A new T2 and/or contrast-enhancing lesions(s) on follow-up MRI, irrespective of its timing **OR** • Await a second clinical attack



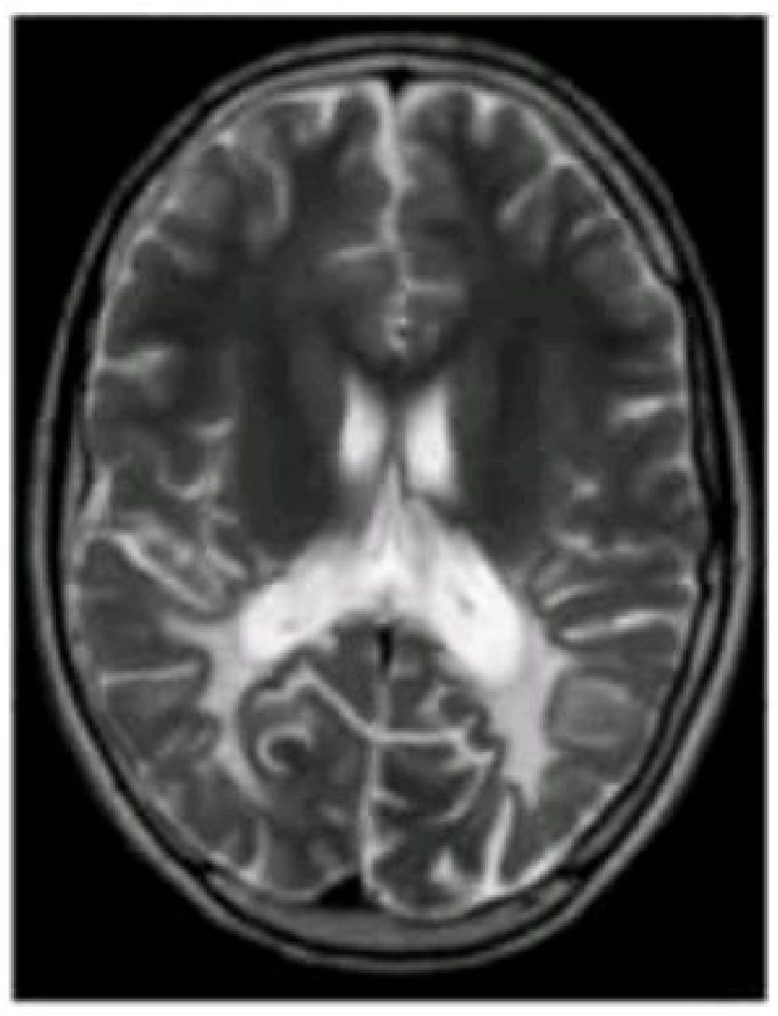
On the left a patient who was re-examined 3 months after the first clinical attack.
Describe the lesions and decide which findings are typical for MS.

Typical findings for MS as seen in this case are:

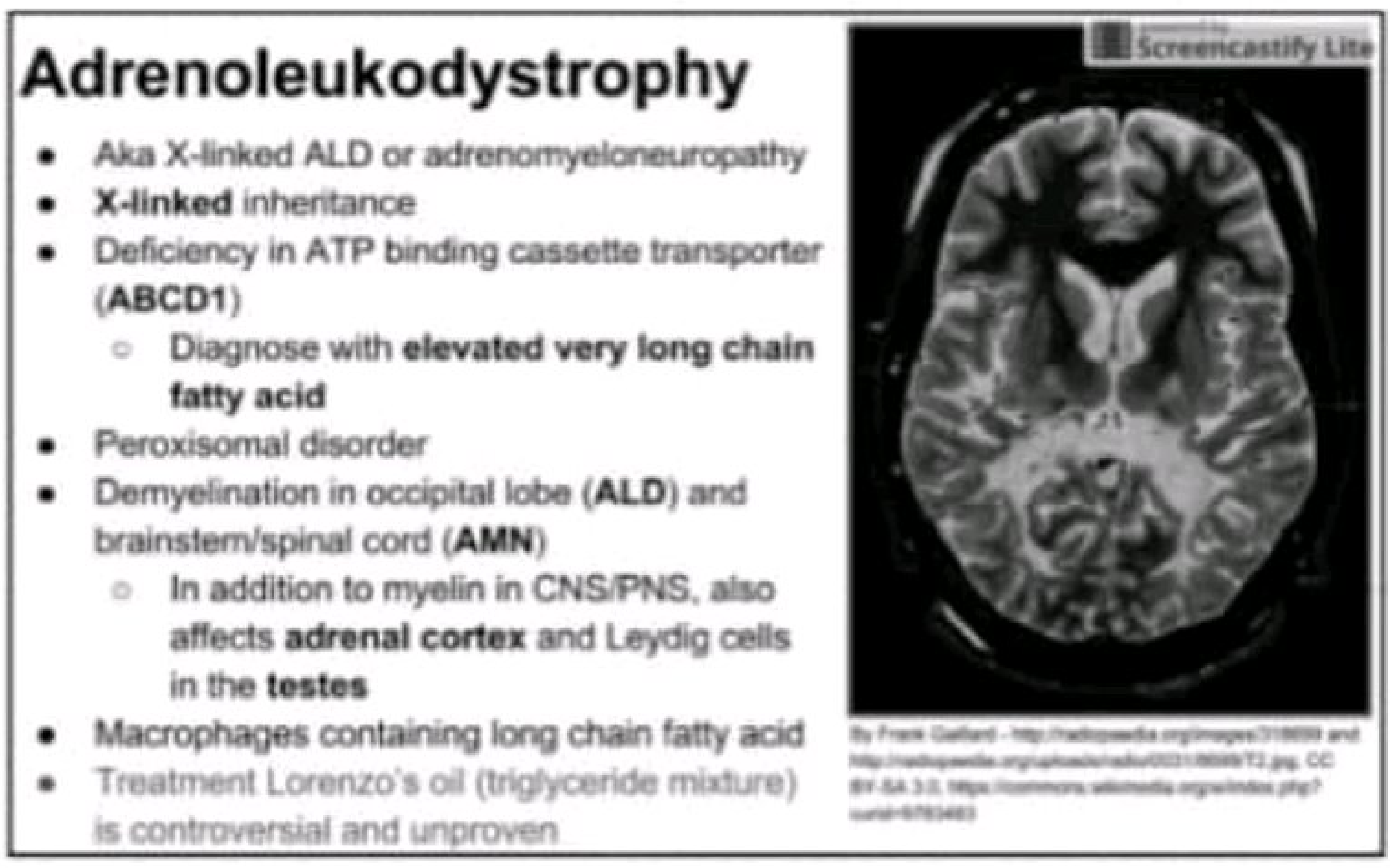
- Multiple enhancing lesions
- Many of these lesions 'touch the cortex' and must be located in the U-fibers.
- These enhancing lesions all are new lesions, since Gadolinium enhancement is only visible for about 1 month.
  So this finding is proof of dissemination in time.

OTHERS DYSMYELINATING DISORDERS

1) X-linked adrenoleukodystrophy



Posterior part involved with sparing of subcortical U Fibres

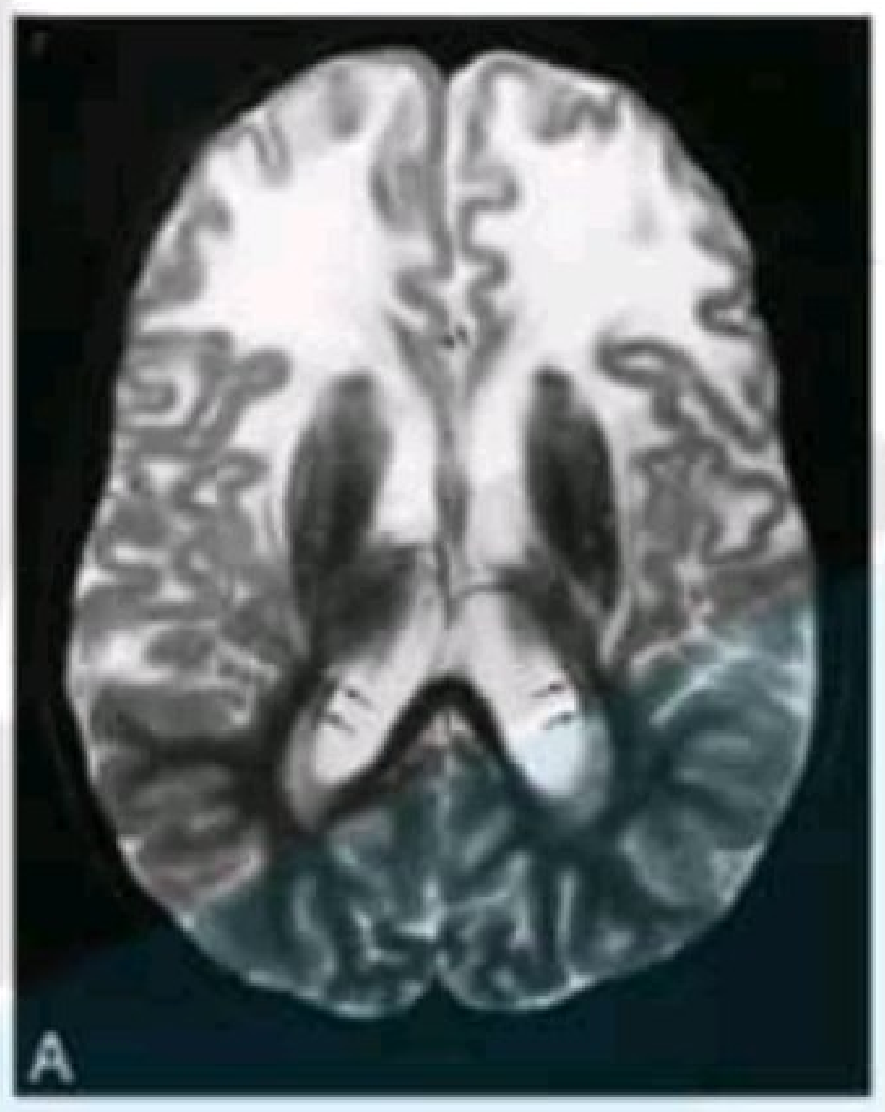


Adrenoleukodystrophy

- Aka X-linked ALD or adrenomyeloneuropathy
- **X-linked** inheritance
- Deficiency in ATP binding cassette transporter (**ABCD1**)
  - Diagnose with **elevated very long chain fatty acid**
- Peroxisomal disorder
- Demyelination in occipital lobe (**ALD**) and brainstem/spinal cord (**AMN**)
  - In addition to myelin in CNS/PNS, also affects **adrenal cortex** and Leydig cells in the **testes**
- Macrophages containing long chain fatty acid
- Treatment Lorenzo's oil (triglyceride mixture) is controversial and unproven

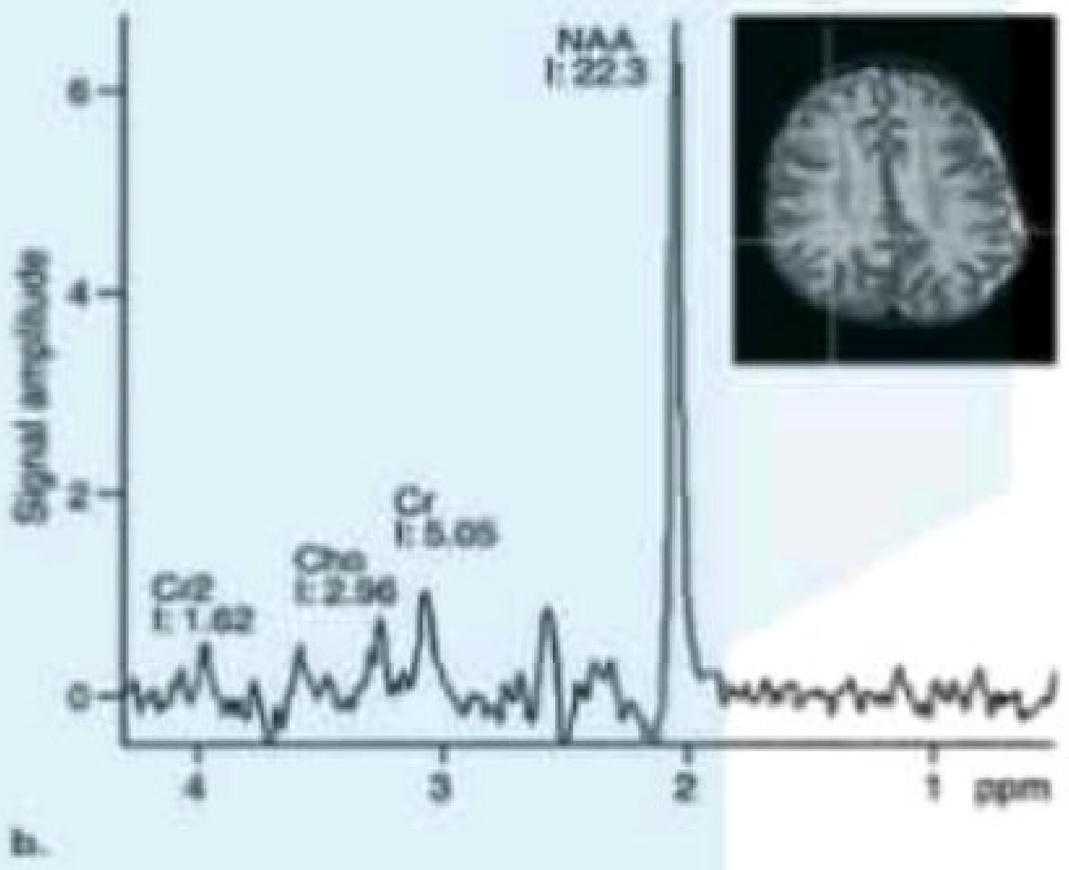
2) ALEXANDER'S Disease

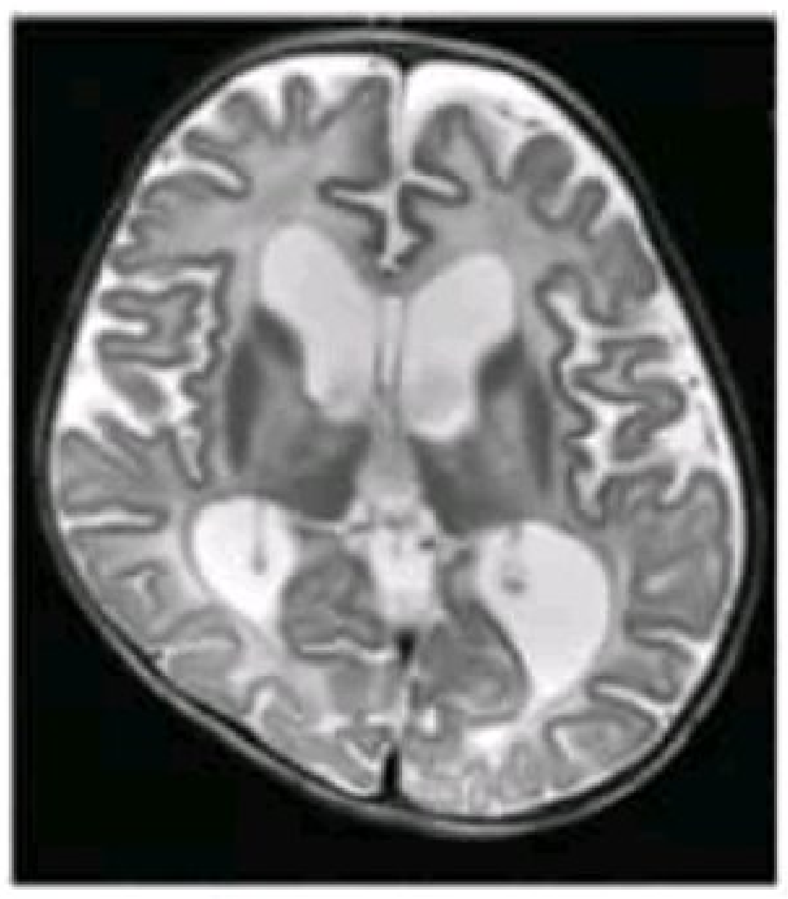
- GFAP mutation
- Clinically Lage head
- Involvement seen primarily in Frontal Lobe
- Presence on Rosenthal fibres on HPE



3) CANAVAN's Disease

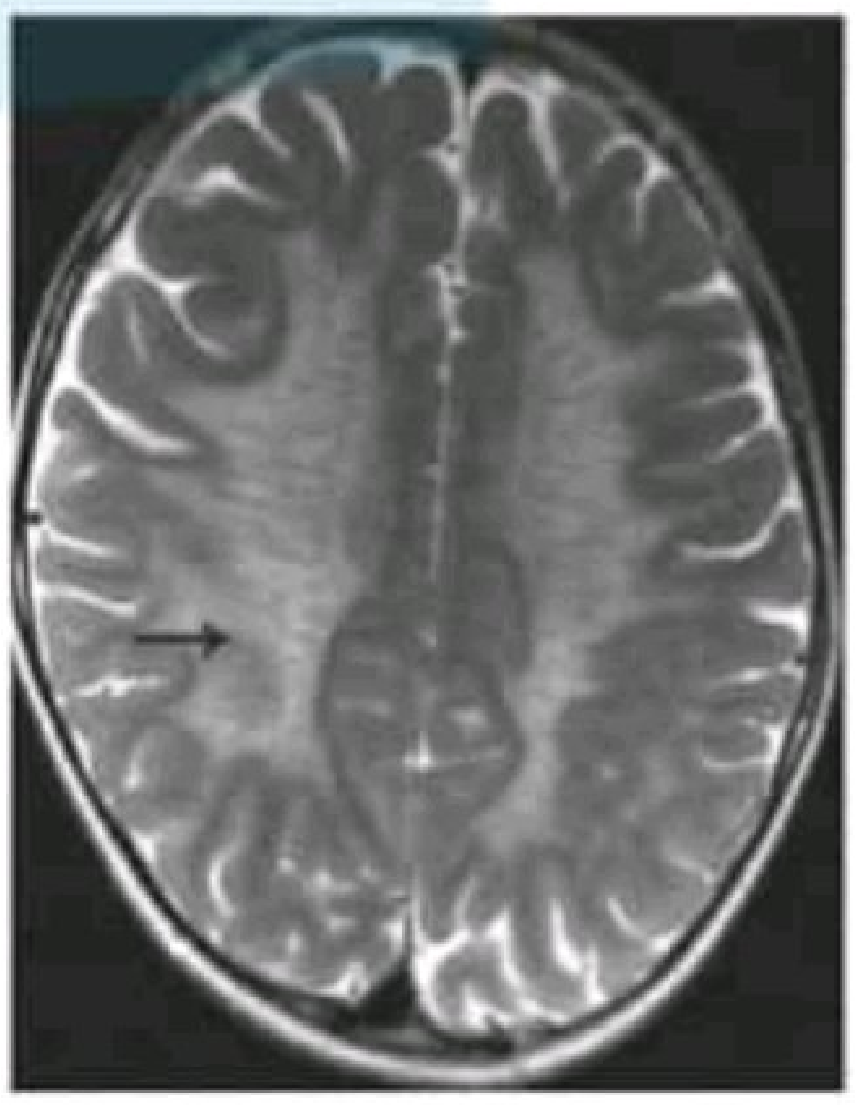
- Clinically Lage head
- Involvement of white matter throught the bone
  (Not any lobe is specifically involved)
- N-Acetyl Aspartate Accumulation





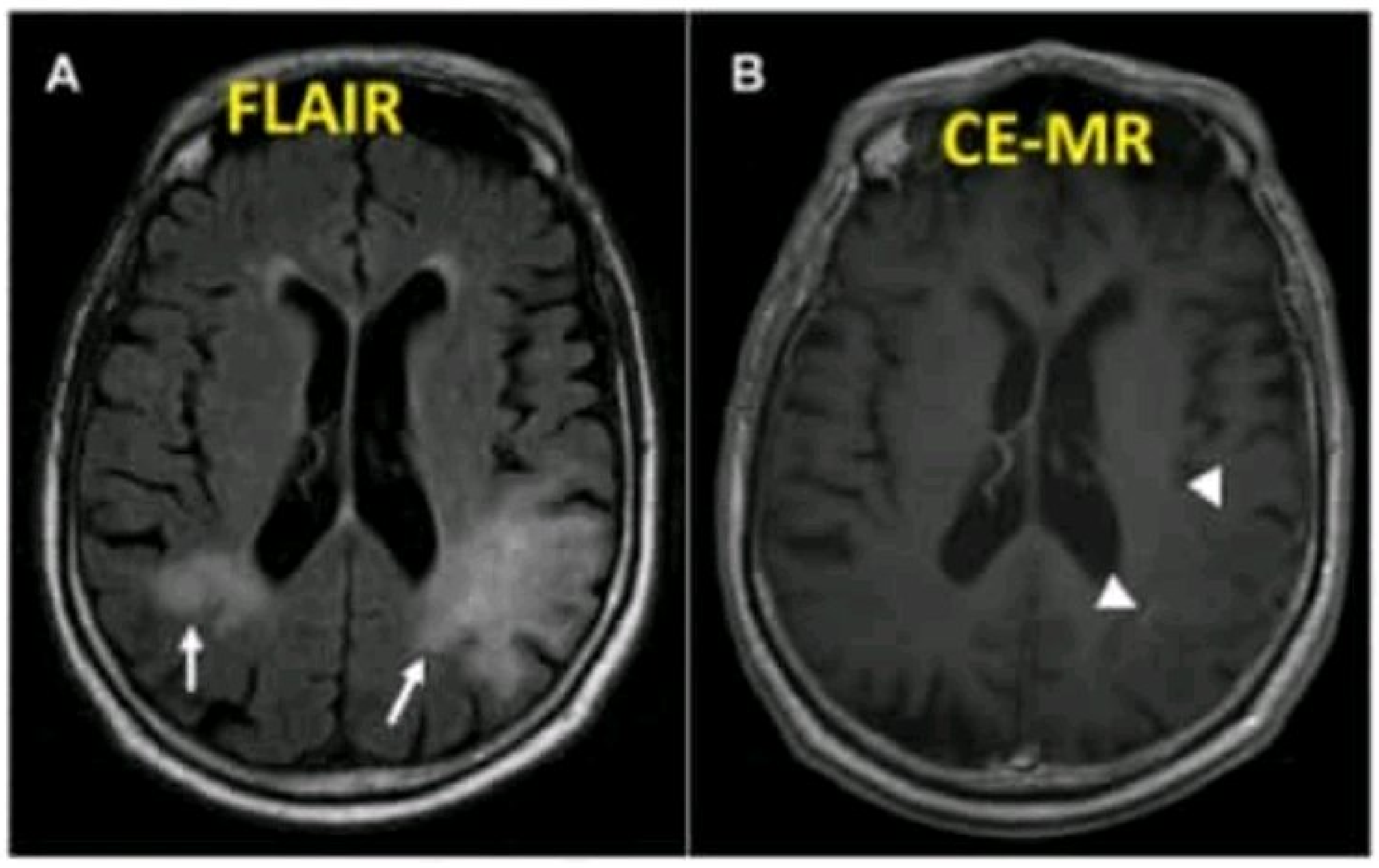
4) Metachromatic Leukodystrophy

- White matter abnormality
- Periventricular sparing: TIGROID PATTERN
- Seen in Children, presenting with developmetal delay



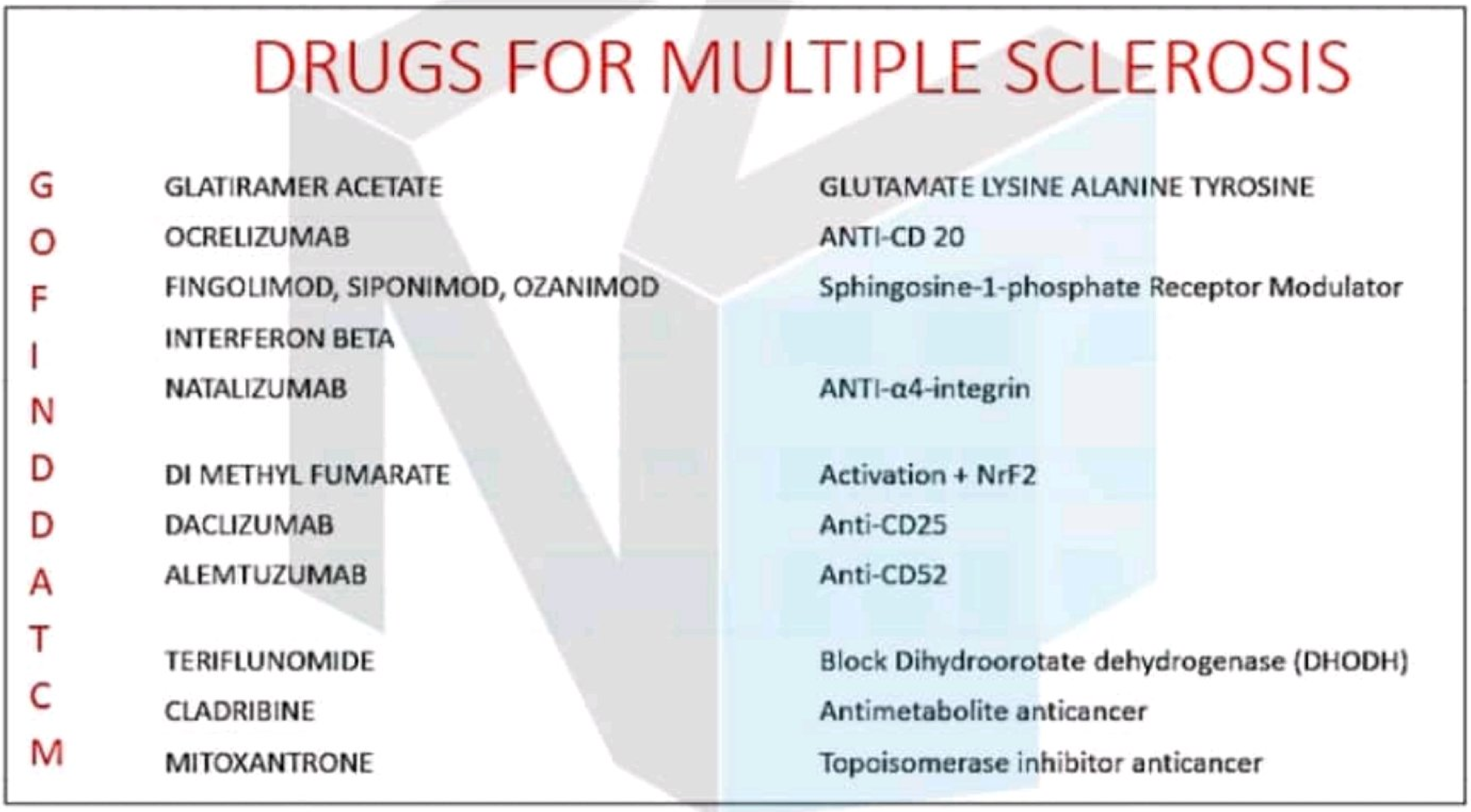
5) Progressive Multifocal Leucoencephalopathy (PML)

- Asymmetric White matter abnormailty in an HIV positive patient
- Enhancing on a FLAIR image but non-enhancing on a CE-MR
- Viral in origin- JC Virus



Pharmacology

- RRMS- All Drugs (Single DOC- Interferon Beta)
- SPMS- MITOXANTRONE > INTERFERONE BETA
- PPMS- OCRELIZUMAB



DRUGS FOR MULTIPLE SCLEROSIS

G	GLATIRAMER ACETATE	GLUTAMATE LYSINE ALANINE TYROSINE
O	OCRELIZUMAB	ANTI-CD 20
F	FINGOLIMOD, SIPONIMOD, OZANIMOD	Sphingosine-1-phosphate Receptor Modulator
I	INTERFERON BETA	
N	NATALIZUMAB	ANTI-α4-integrin
D	DI METHYL FUMARATE	Activation + NrF2
D	DACLIZUMAB	Anti-CD25
A	ALEMTUZUMAB	Anti-CD52
T	TERIFLUNOMIDE	Block Dihydroorotate dehydrogenase (DHODH)
C	CLADRIBINE	Antimetabolite anticancer
M	MITOXANTRONE	Topoisomerase inhibitor anticancer

- Maximum improvement in EDSS Scale in Multiple Sclerosis→ MITOXANTRONE> NATALIZUMAB
- NATALIZUMAB S/E: PML (JC Polyoma Virus)
- MODAFINIL: Improves fatigue
- FALFAMPRIDINE (AMINOPYRIDINE): K+ Channel blockers → improves Gait

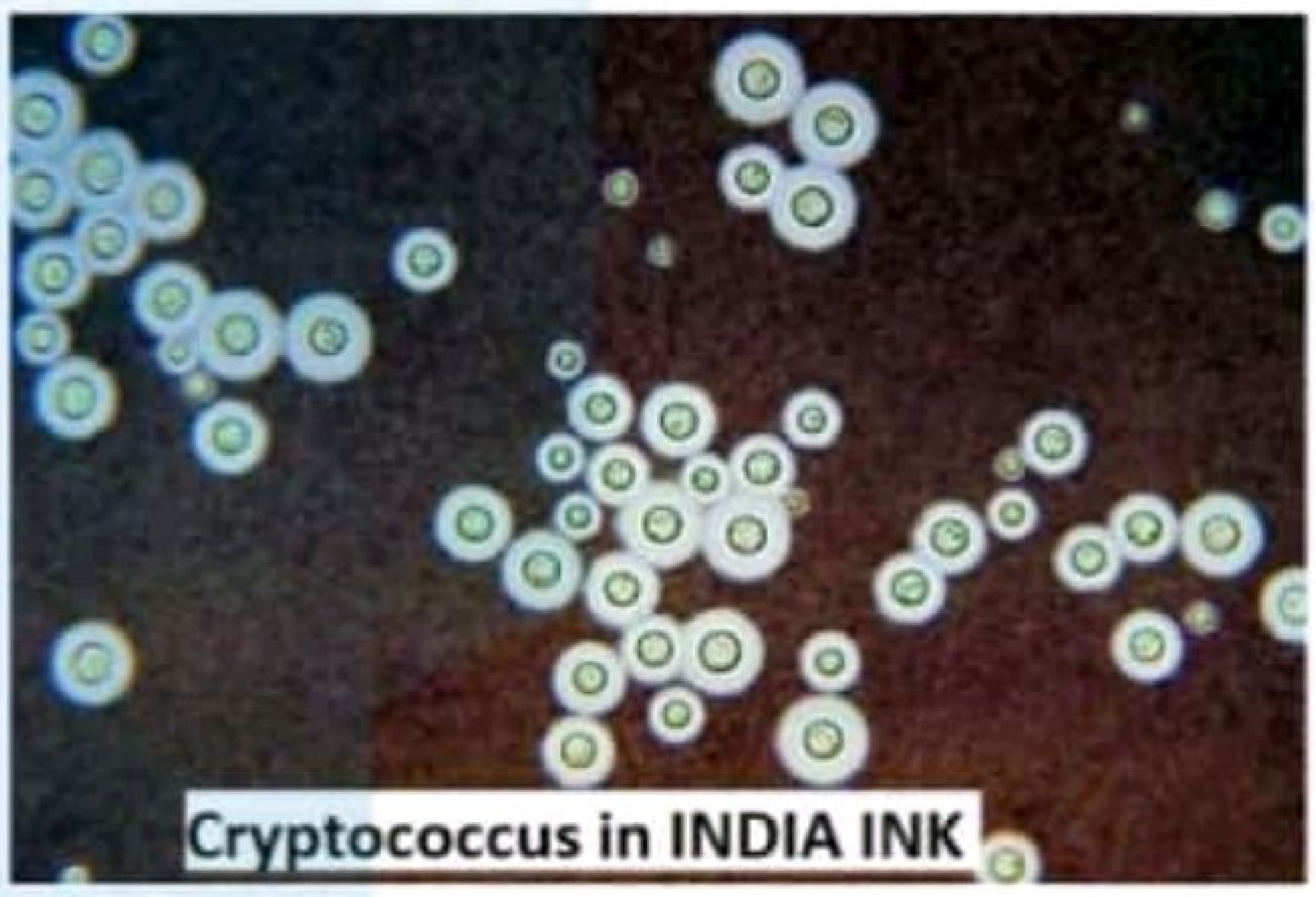
CNS Infections

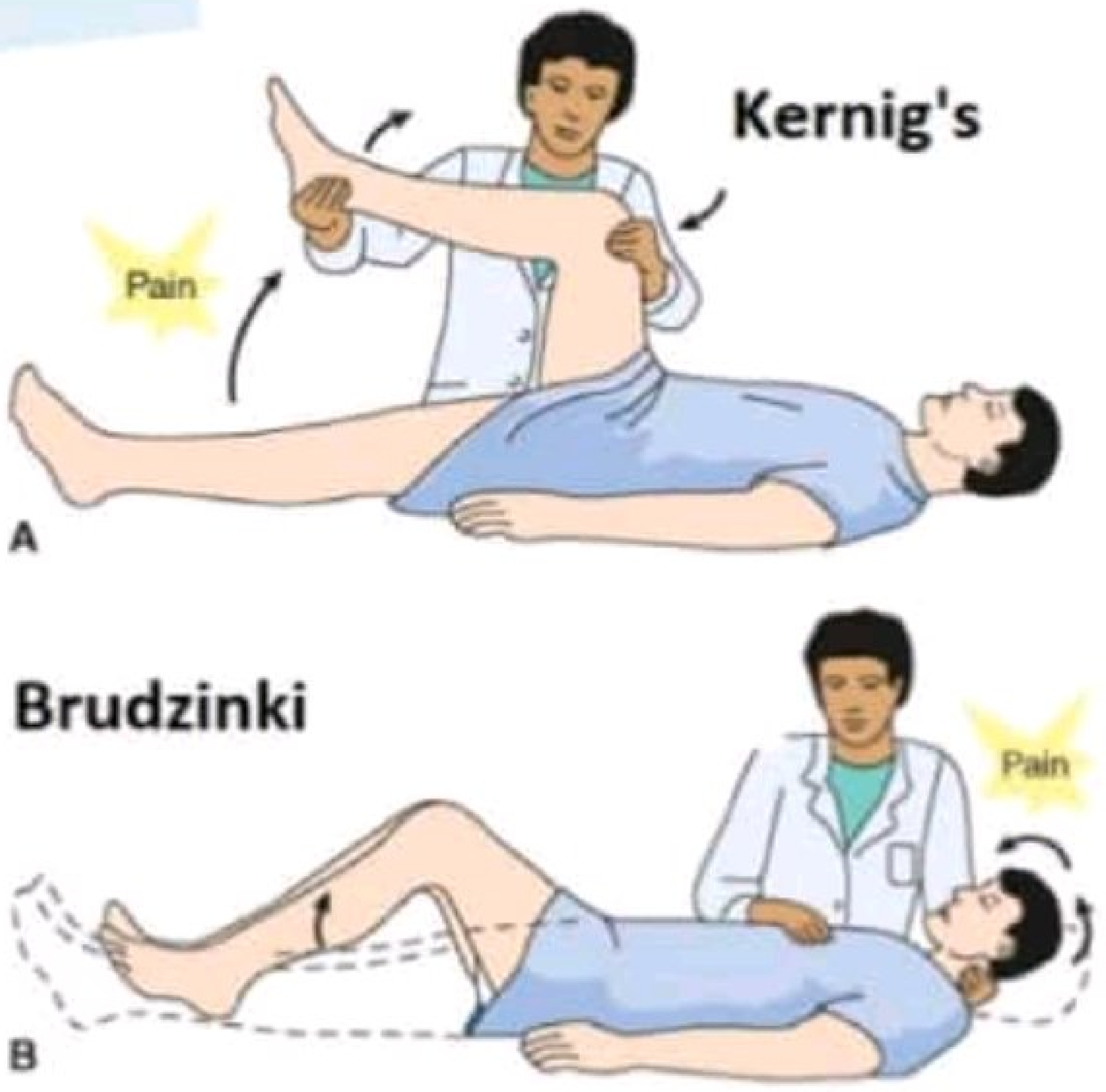
CSF Analysis

Feature	Acute pyogenic	Aseptic	Chronic (TB/Fungal)
Gross Appearance	Cloudy/ Purulent	Clear / Slightly turbid	Turbid/ Cobweb formation(fibrin Coagulum)
Pressure (60-150 mm of H20)	Slightly increased (>180)	Moderate increase (>250)	Highly increased(>300)
Cells(0-4/ml)	1-10,000/ml (Neutrophil predominant)	10-100/ml (Lymphocytes predominant)	100-1000/ml (lymphocyte predominant)
Proteins (15-45 mg/dl)	Increased	Increased	Increased
Glucose (50-80 mg/dl)	Reduced (<40)	Normal	Reduced
Bacteriology	Bacteria +	Sterile	AFB+
Other investigations	Culture Gold standard	PCR gold standard	Culture for TB India ink (for cryptococcal)

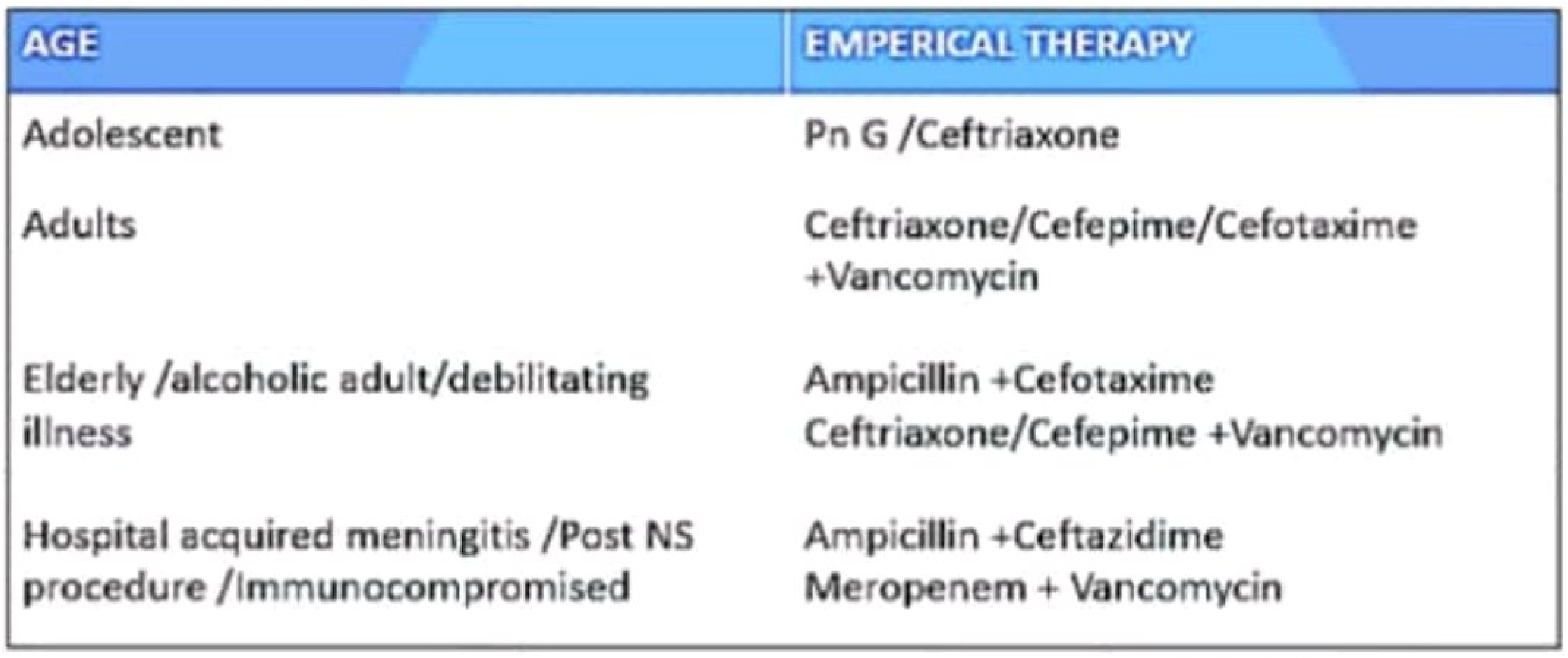
Pyogenic Meningitis

- Most Common Cause
    - Adoloscent/epidemic- N. meningitidis
    - Adult/Elderly/Community acquired is S. Pnuemoniae
    - In developing countries: TB
- Clinical Features:
    - Fever
    - Headache
    - Neck Rigidity
    - + Altered Sensorium
- Treatment: Empirical Therapy
    - DEXAMETHASON should be given prior to any antibiotics, so as to decrease the cerebral edema and improve the penetration of any antibiotic to be given.
    - Antibiotic duration
        - Adoloscent- 7 days
        - Adults- 14 days
        - Listeria – Ampicillin 21 days


Cryptococcus in INDIA INK


Kernig's

Brudzinki



AGE	EMPERICAL THERAPY
Adolescent	Pn G /Ceftriaxone
Adults	Ceftriaxone/Cefepime/Cefotaxime +Vancomycin
Elderly /alcoholic adult/debilitating illness	Ampicillin +Cefotaxime Ceftriaxone/Cefepime +Vancomycin
Hospital acquired meningitis /Post NS procedure /Immunocompromised	Ampicillin +Ceftazidime Meropenem + Vancomycin

Neuro-tuberculosis

1. **Tubercular Meningitis Basal/Spinal** **(M/C Neuro TB- Basal TBM)**
2. **Tuberculoma intracranial/spinal**
3. **TB Abscess**
4. **TB encephalopathy**

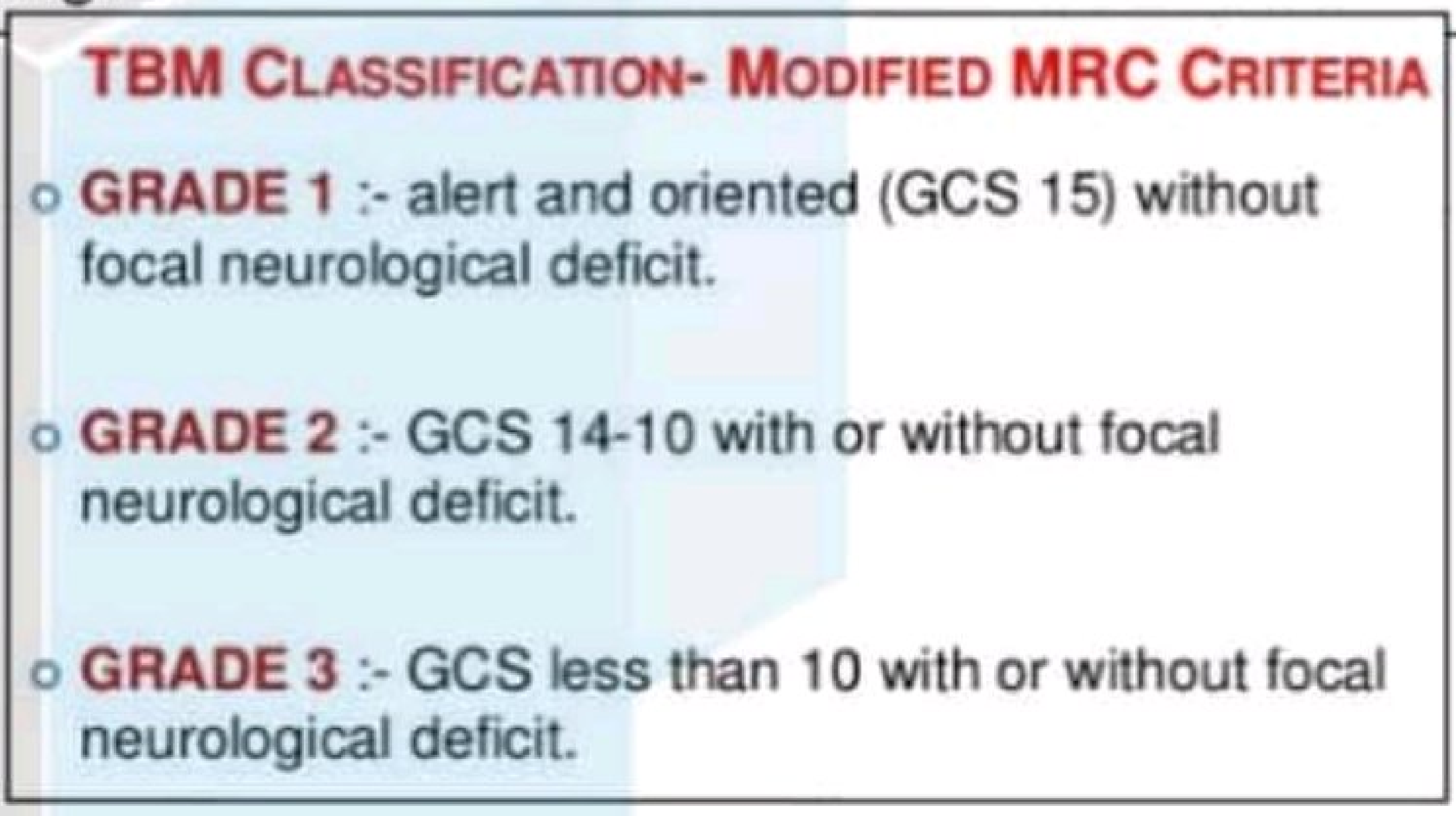
LESIONS

1) Meningeal exudates @base of the brain
2) Vasculopathy –medium ,large sized arteries –Infarct (MC in MCA)
3) Border zone encephalitis
4) Hydrocephalus –obstructive
5) Tuberculoma –liq.necrosis
6) TB encephalopathy
7) Spinal meningitis

M/C Lesion- Meningeal Exudates

Treatment:

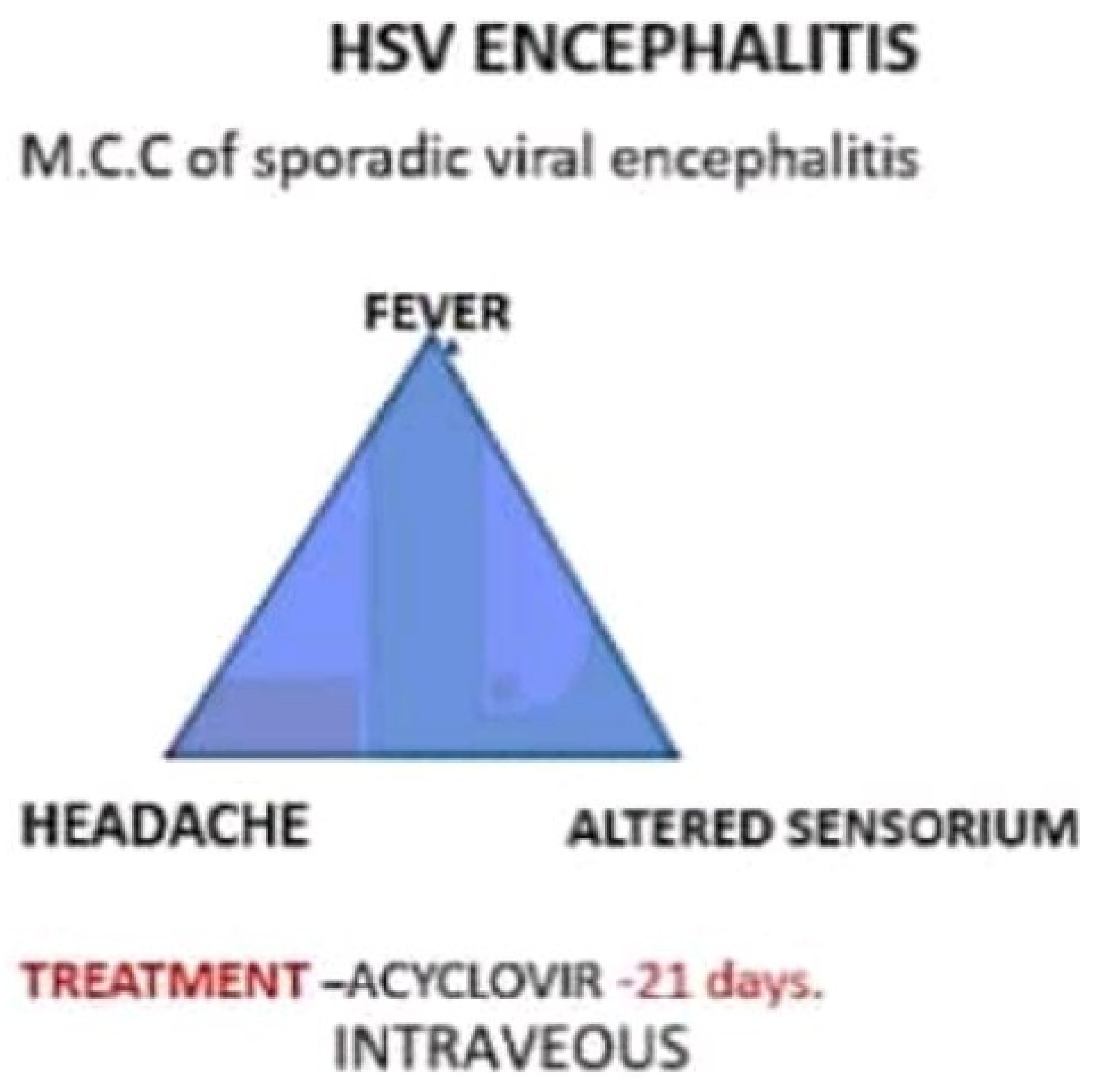
- HRZS x 2 months, HR x 10 months Total 12 months. Can extend to 18 months.
- Steroids- Dexamethasone



TBM CLASSIFICATION- MODIFIED MRC CRITERIA

- **GRADE 1** :- alert and oriented (GCS 15) without focal neurological deficit.
- **GRADE 2** :- GCS 14-10 with or without focal neurological deficit.
- **GRADE 3** :- GCS less than 10 with or without focal neurological deficit.

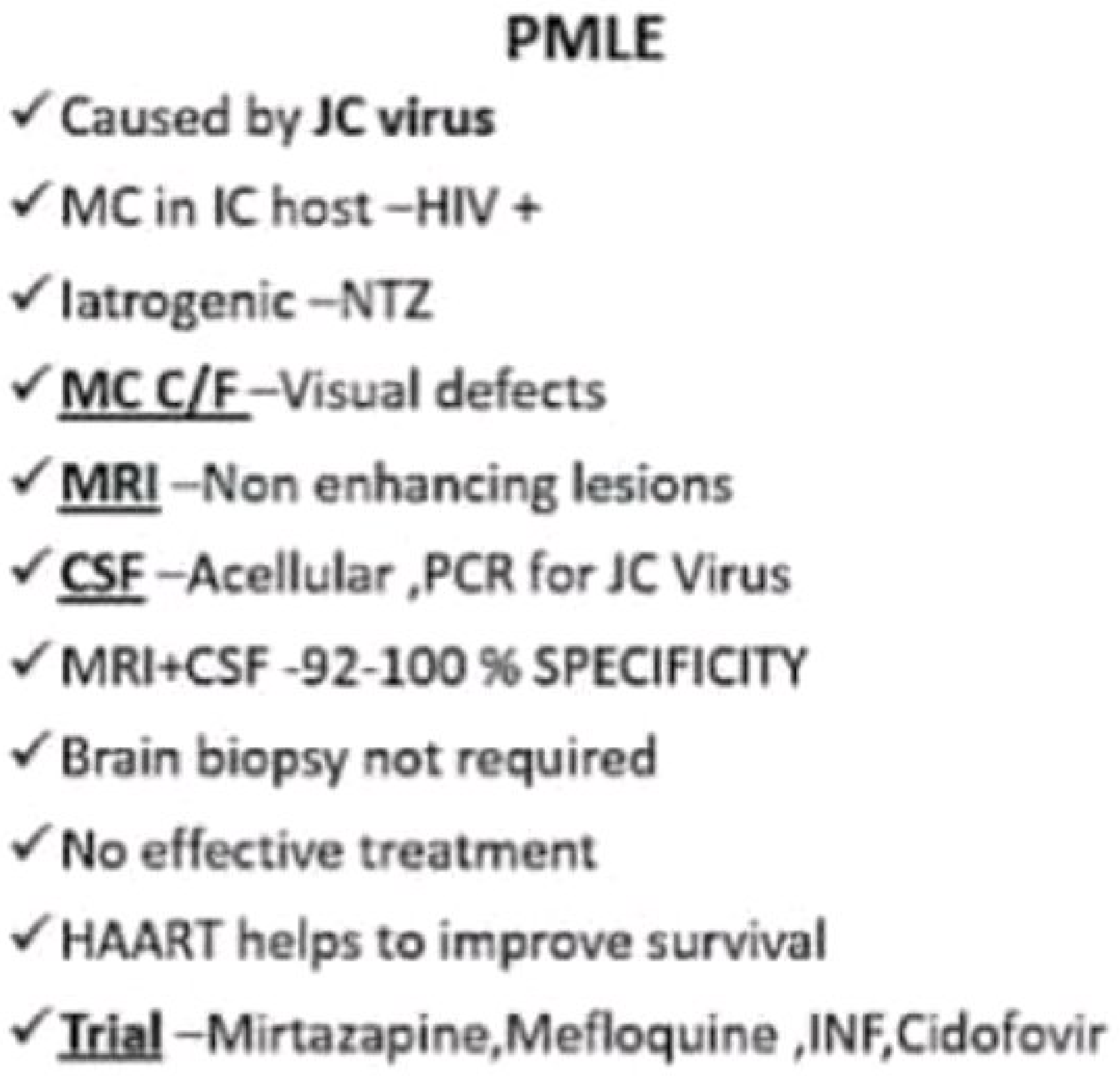
VIRAL INFECTIONS



HSV ENCEPHALITIS

M.C.C of sporadic viral encephalitis

TREATMENT –ACYCLOVIR -21 days.
INTRAVEOUS



PMLE

✓Caused by **JC virus**
✓MC in IC host –HIV +
✓Iatrogenic –NTZ
✓MC C/F –Visual defects
✓MRI –Non enhancing lesions
✓CSF –Acellular ,PCR for JC Virus
✓MRI+CSF -92-100 % SPECIFICITY
✓Brain biopsy not required
✓No effective treatment
✓HAART helps to improve survival
✓Trial –Mirtazapine,Mefloquine ,INF,Cidofovir

0.4mg/kg/day over 6-8 weeks (to prevent vasculopathy)

CRYPTOCOCCAL MENINGITIS

- MCC meningitis in HIV +
- Enter via lung –Asymtomatic pn
- No signs of meningitis in early stage
- CSF – Mild pleocytosis
  India Ink staining

MRI –Enlarged Virchow robin spaces
Treatment
Induction therapy –Amphotericin B
+Flucytosine
Maintenance –Fluconazole

TOXOPLASMOSIS

- M.C focal mass lesion in HIV +
- Acquired via –Uncooked meat ,cat feaces
- Headache,fever,FND,altered sensorium
- Serum IgG abs + with CD4 count <200
- LP –Contraindicated
- Treatment

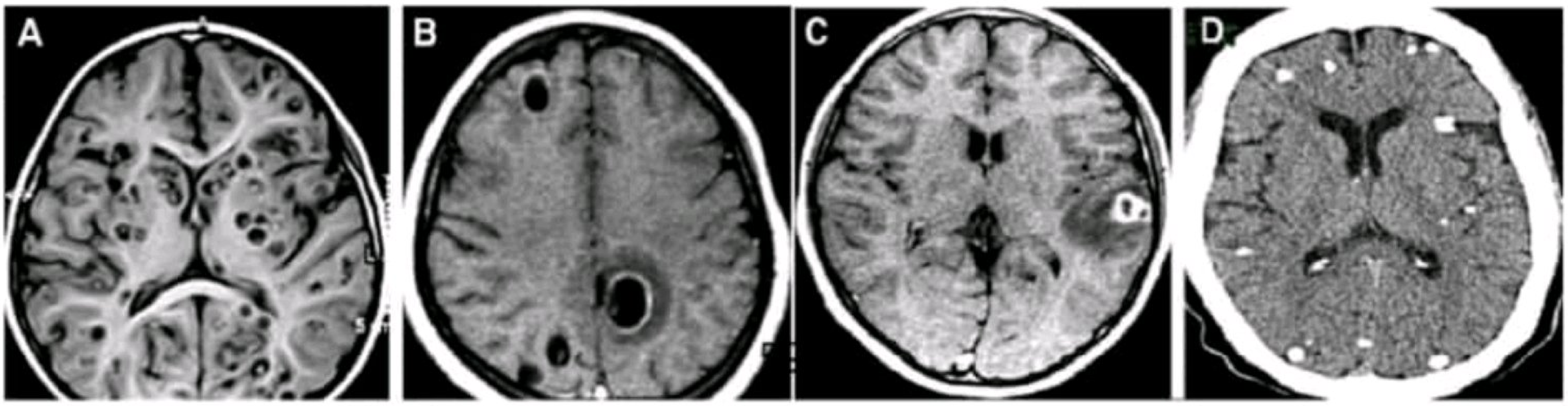
Induction treatment
Pyrimethamine+sulfadiazine+Leucovorin
OR
Trimethoprim +sulfathiazole

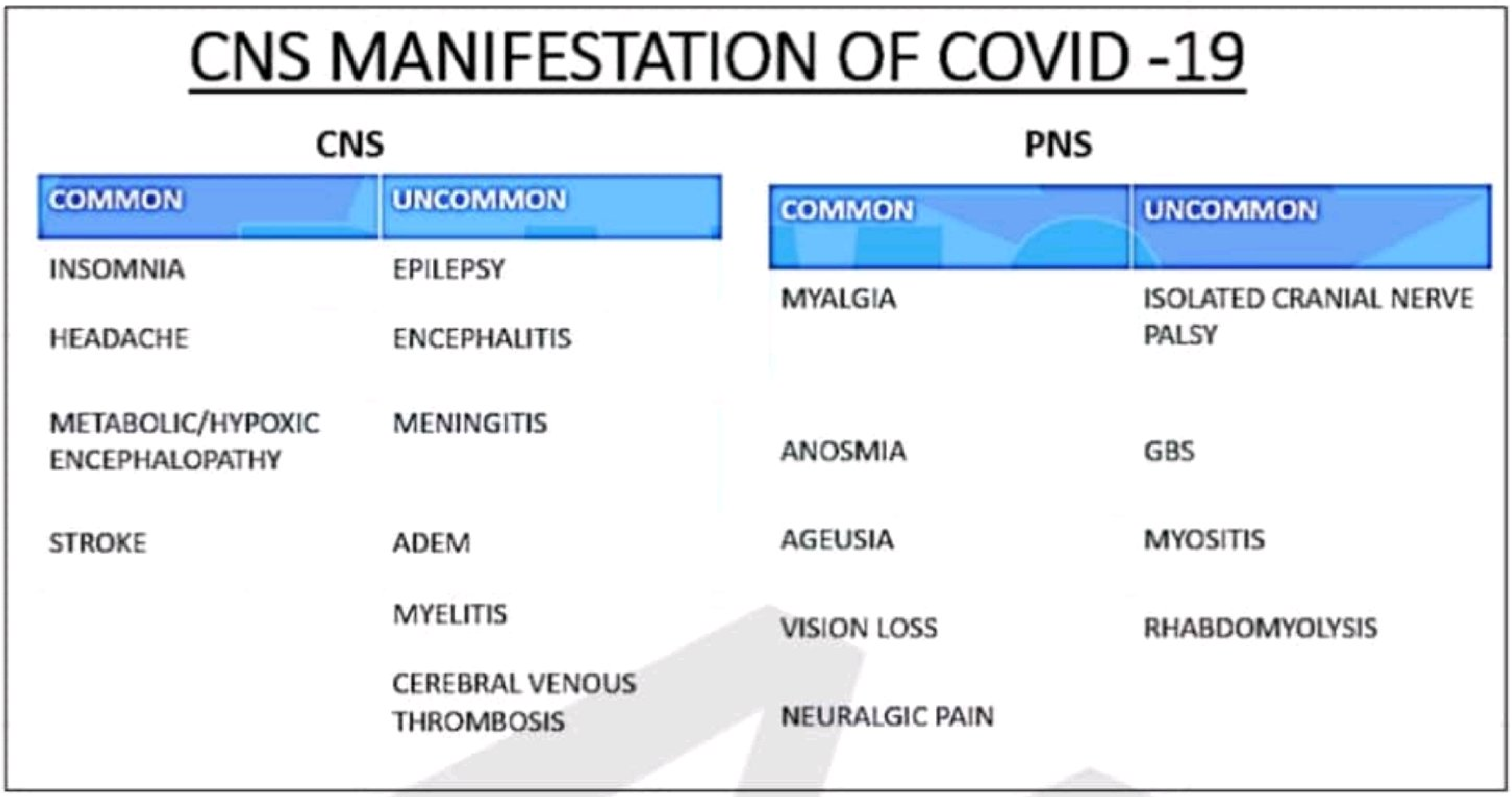
Neurocysticercosis

- Agent –Taenia solium
- M.C site –Intraparenchymal > Subarachnoid
- M.C c/f – Seizure
- Investigation –Imaging /CSF
- Treatment
  - Albendazole @15mg/kg/day X8-28 days +Steroids
  - C/I in spinal, ocular, muscular & disseminated cysticercosis (Multiple ring enhancing lesions with live scolex of Taenia within them)
- Radiology: DECIDES THE DRUG TO BE GIVEN

There are four main stages (also known as **Escobar's pathological stages**):

A. **vesicular**: viable parasite with intact membrane and therefore no host reaction.
B. **colloidal vesicular**: parasite dies within 4-5 years 1 untreated, or earlier with treatment and the cyst fluid becomes turbid. As the membrane becomes leaky edema surrounds the cyst. This is the most symptomatic stage.
C. **granular nodular**: edema decreases as the cyst retract further; enhancement persists.
D. **nodular calcified**: end-stage quiescent calcified cyst remnant; no edema.





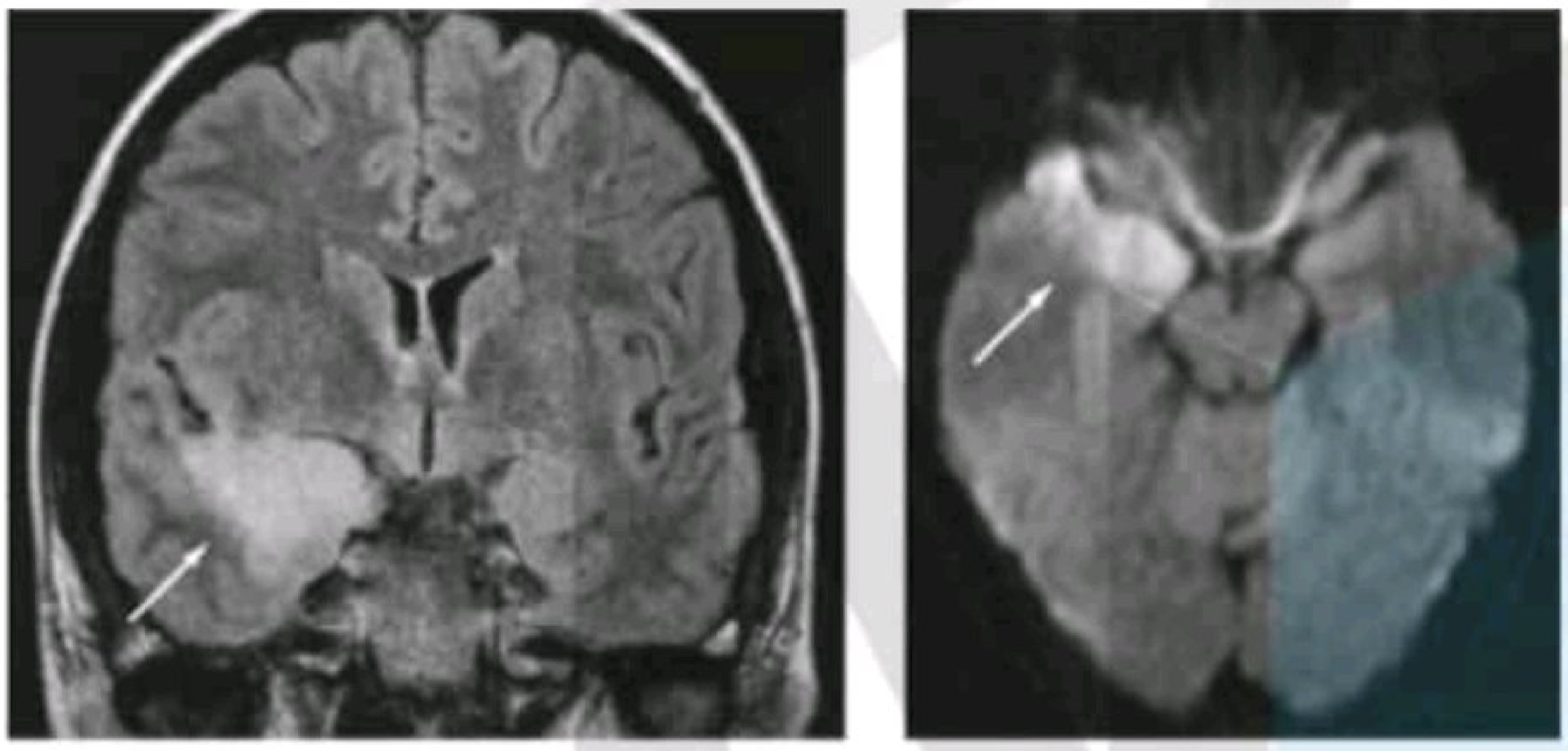
CNS MANIFESTATION OF COVID -19

CNS

COMMON	UNCOMMON
INSOMNIA	EPILEPSY
HEADACHE	ENCEPHALITIS
METABOLIC/HYPOXIC ENCEPHALOPATHY	MENINGITIS
STROKE	ADEM
	MYELITIS
	CEREBRAL VENOUS THROMBOSIS

PNS

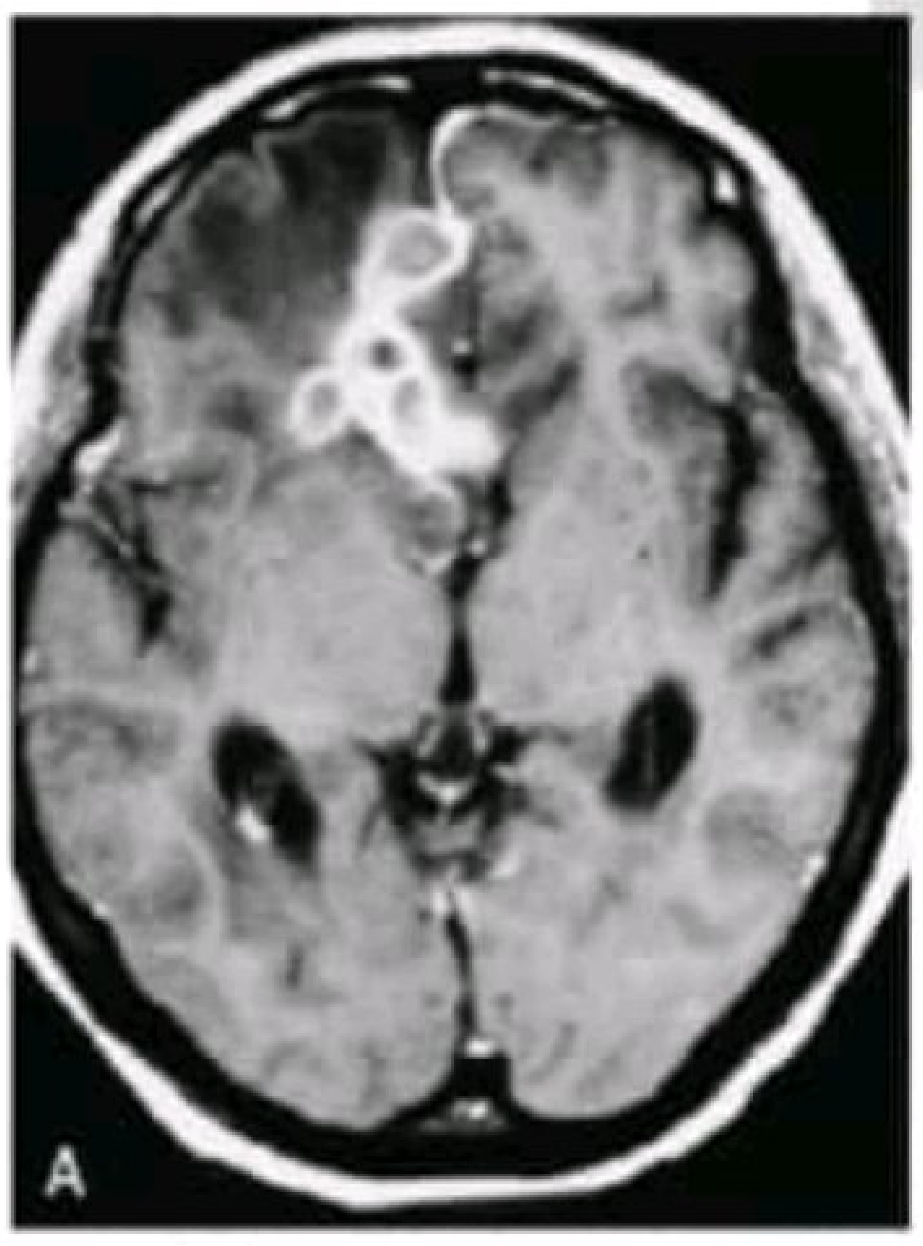
COMMON	UNCOMMON
MYALGIA	ISOLATED CRANIAL NERVE PALSY
ANOSMIA	GBS
AGEUSIA	MYOSITIS
VISION LOSS	RHABDOMYOLYSIS
NEURALGIC PAIN	



HSV Encephalitis

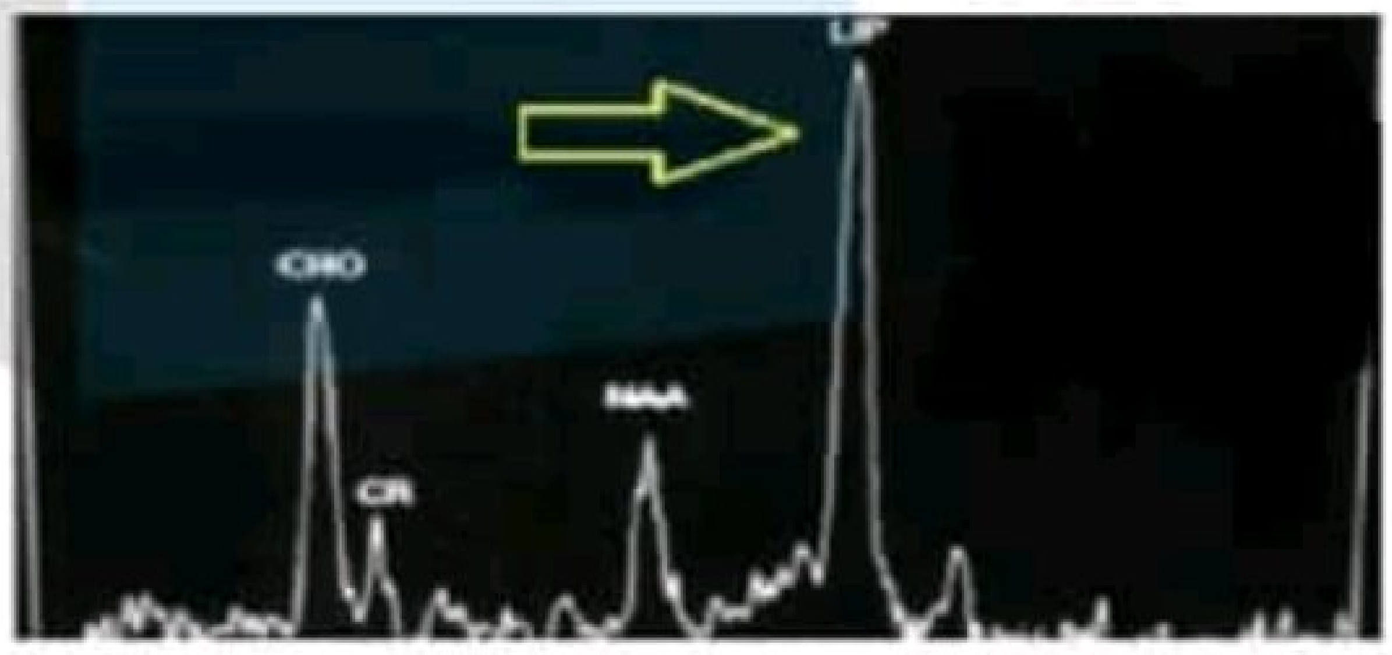
- Temporal lobe involvement specifically

-cingulate gyrus can also be involved.

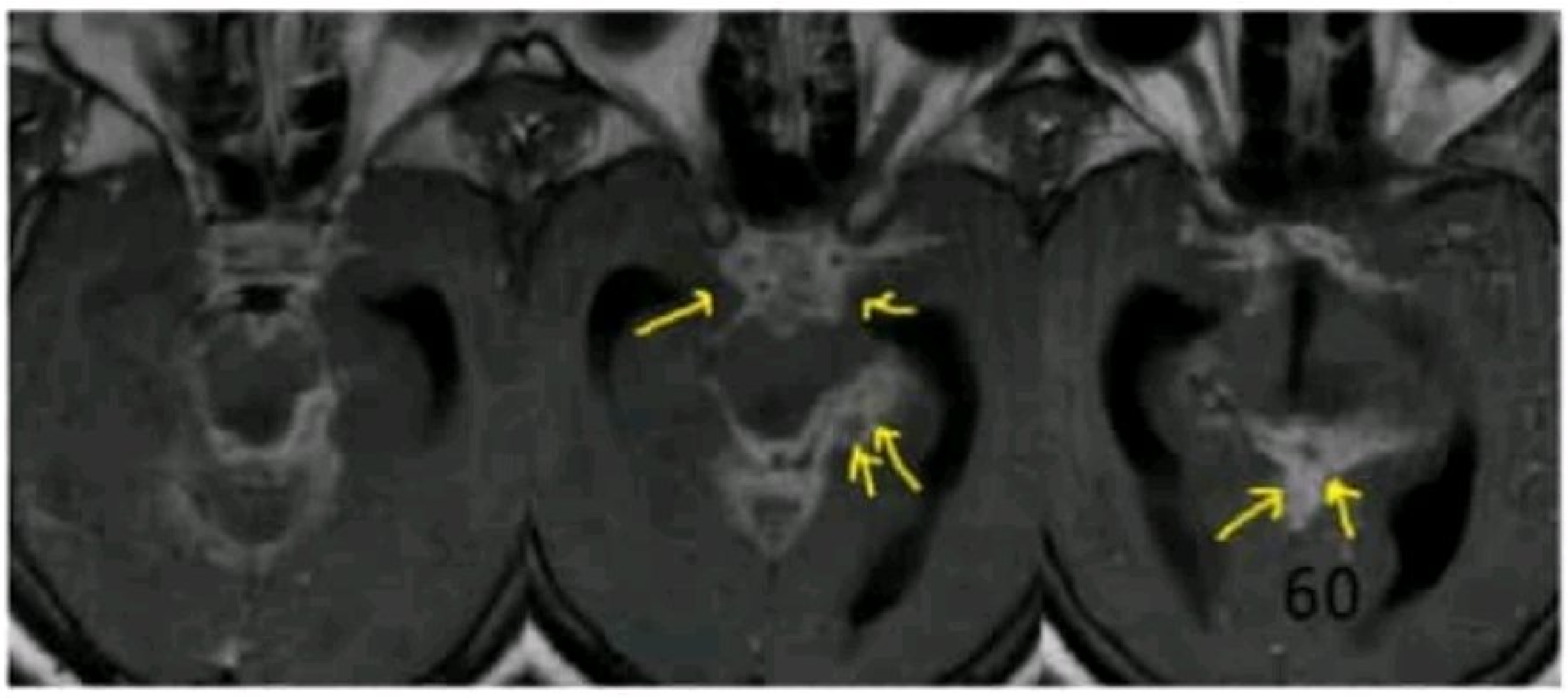


Conglonmerate Ring lesion

Seen in Tuberculomas



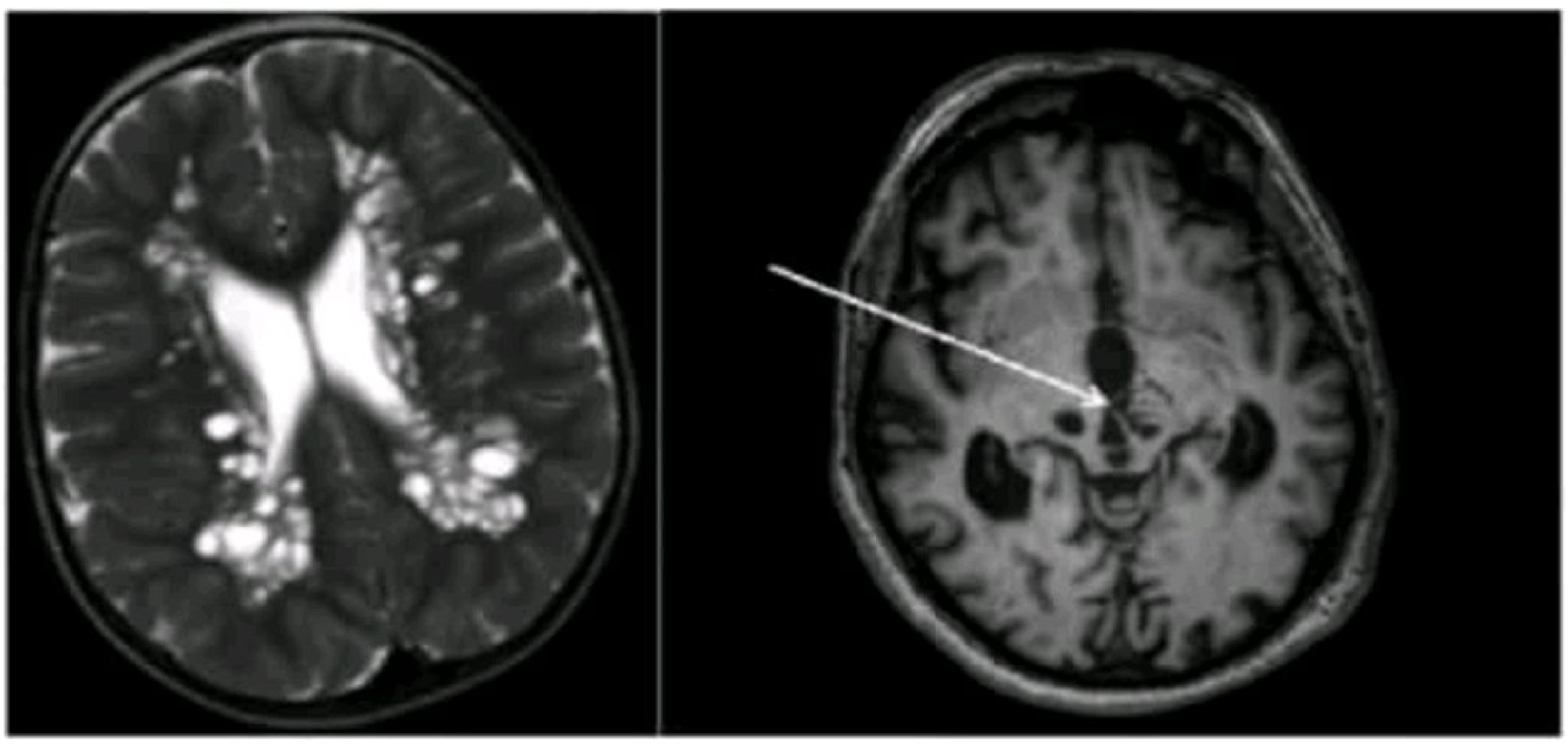
Lipid peak seen on MR Spectroscopy (also seen in Toxoplasma)



Basal Exudates

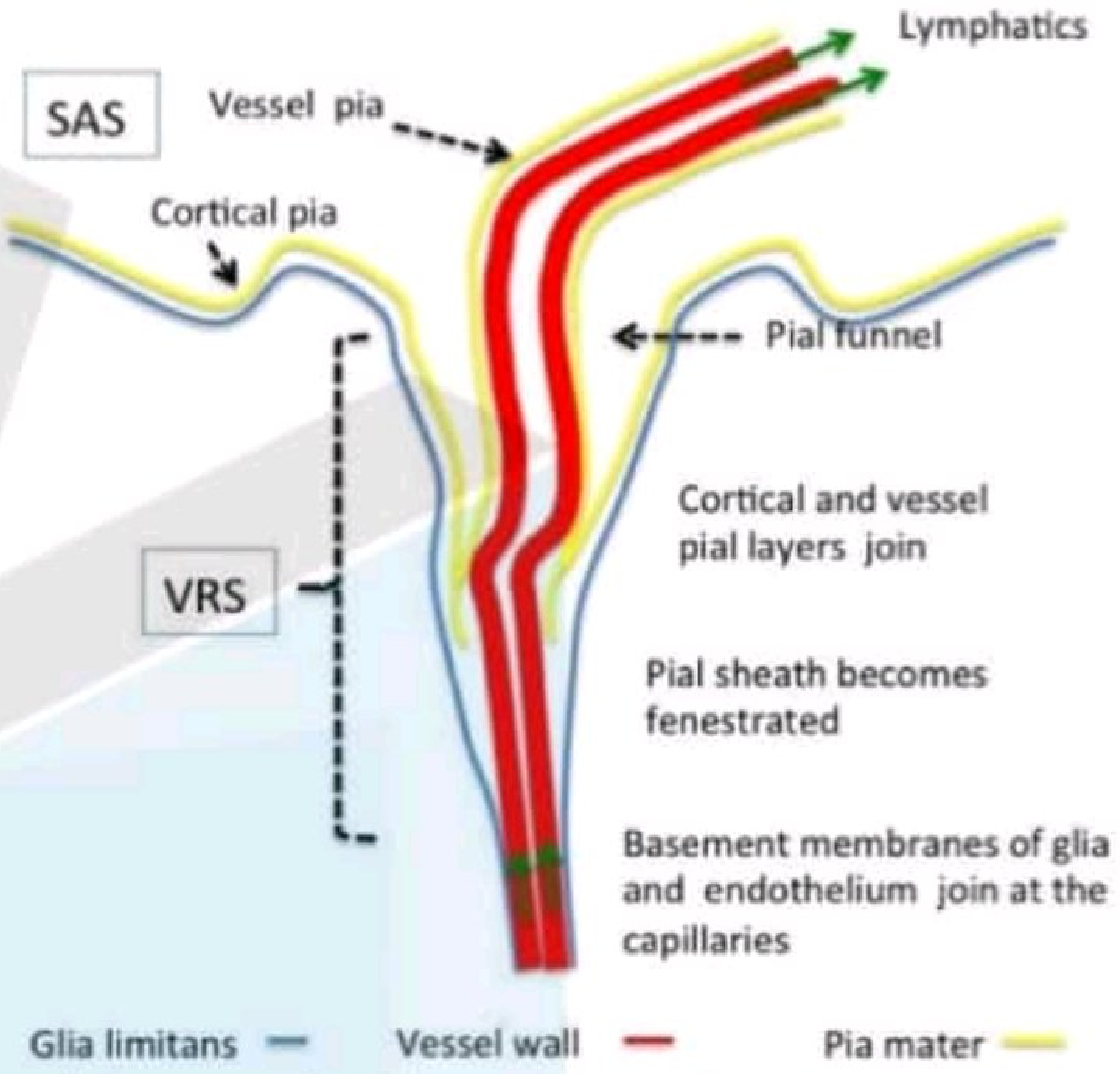
seen in TB Meningitis

on CE-MR

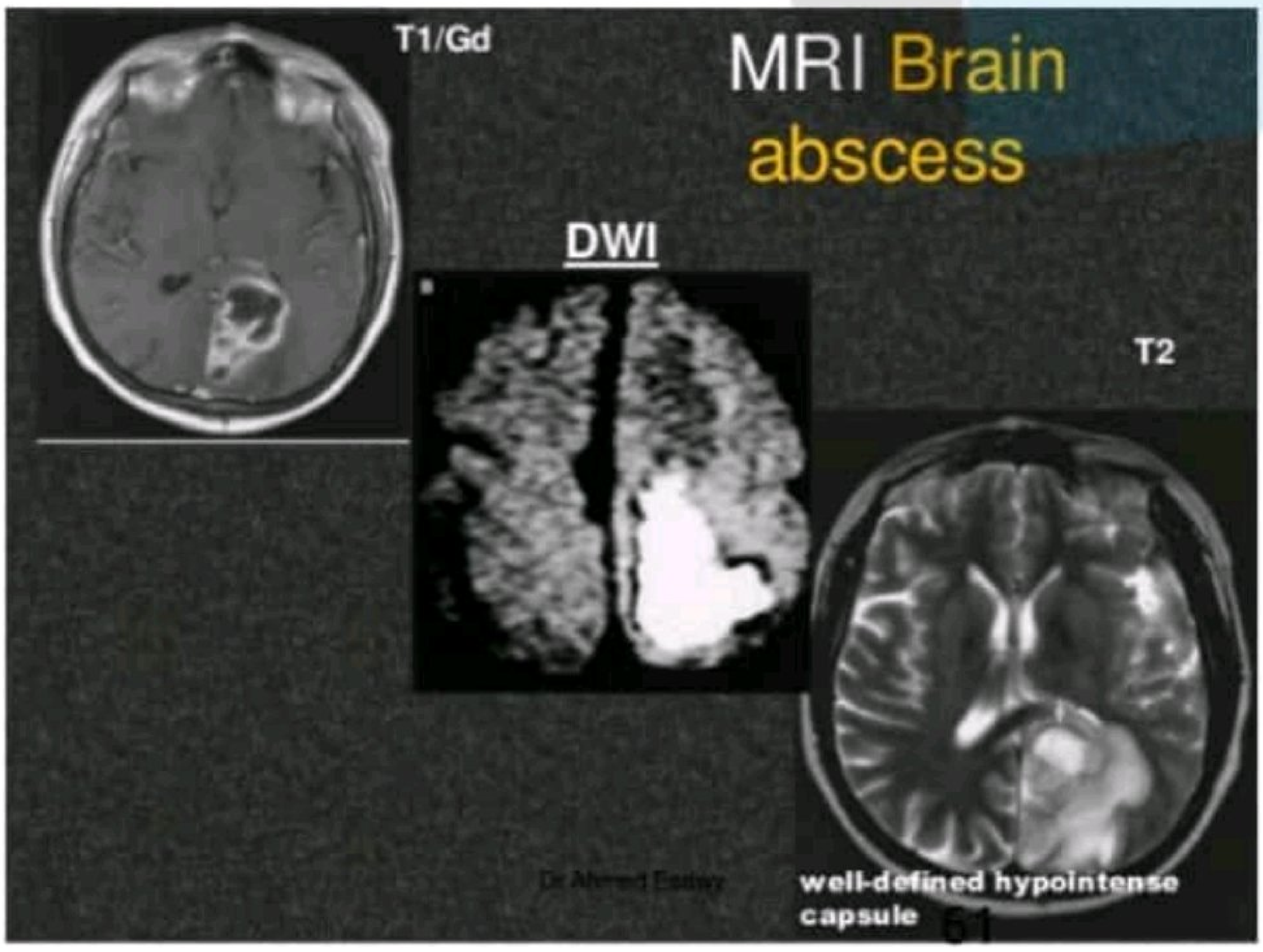


Virchow- Robin Space dilation

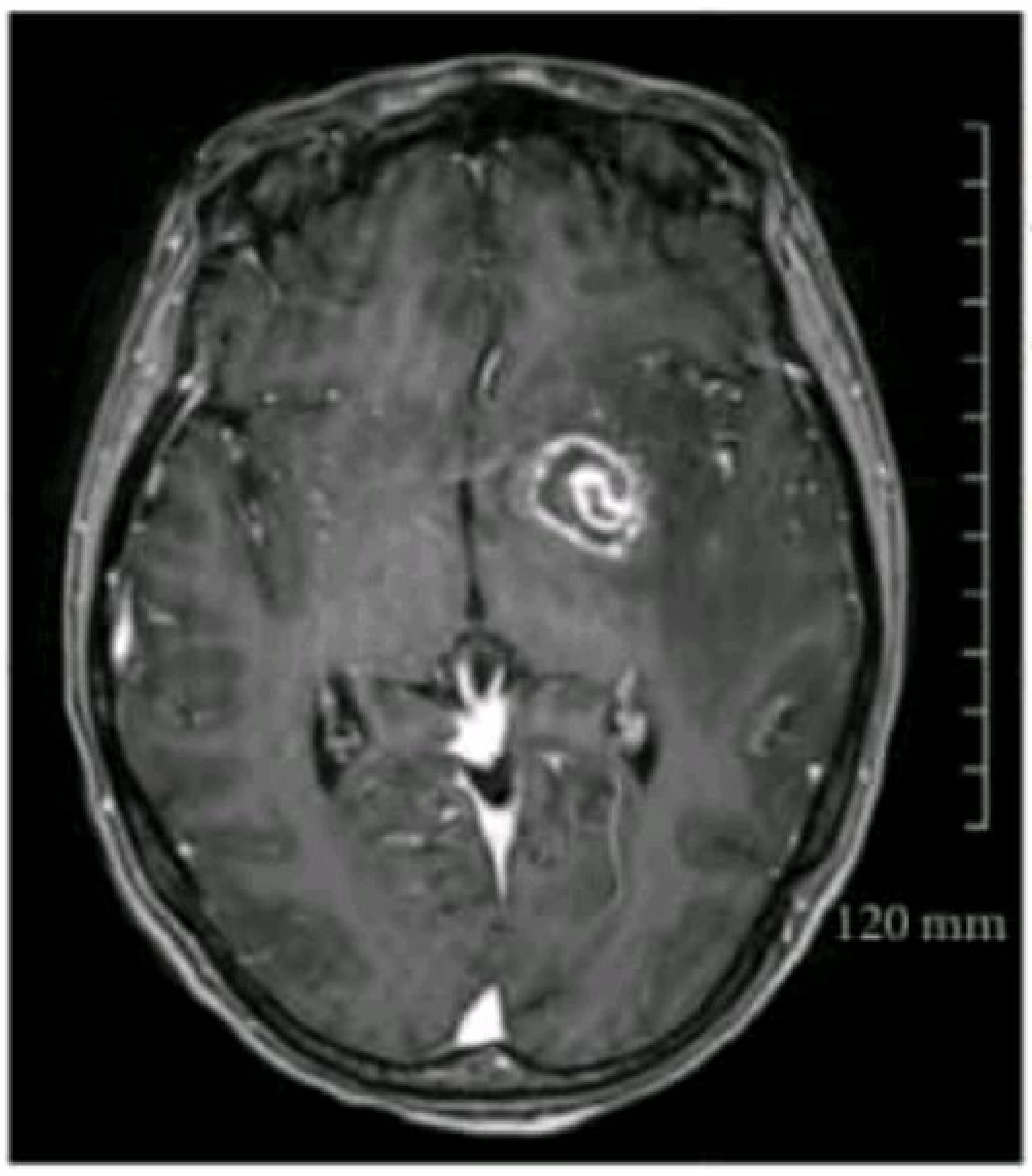
Seen in Cryptococcus


Lymphatics
SAS
Vessel pia
Cortical pia
Pial funnel
VRS
Cortical and vessel pial layers join
Pial sheath becomes fenestrated
Basement membranes of glia and endothelium join at the capillaries
Glia limitans
Vessel wall
Pia mater

Morphology of Virchow Robin and perivascular spaces. Delineated by basal membranes of glia, pia and endothelium, the Virchow Robin space (VRS) depicts the space surrounding vessels penetrating into the parenchyma. The VRS is obliterated at the capillaries where the basement membranes of glia and endothelium join. The complex pial architecture may be understood as an invagination of both cortical and vessel pia into the VRS. The pial funnel is not a regular finding. The pial sheath around arteries extends into the VRS, but becomes more fenestrated and eventually disappears at the precapillary section of the vessel. Unlike arteries (as shown in this figure), veins do not possess a pial sheath inside the VRS. ISF may drain by way of an intramural pathway along the basement membranes of capillaries and arterioles into the lymphatics at the base of the skull (green arrows).


MRI Brain abscess
T1/Gd
DWI
T2
Dr Ahmed Essawy
well-defined hypointense capsule

Brain Abscess: Ring Enhancing lesion which is bright on DW-MRI

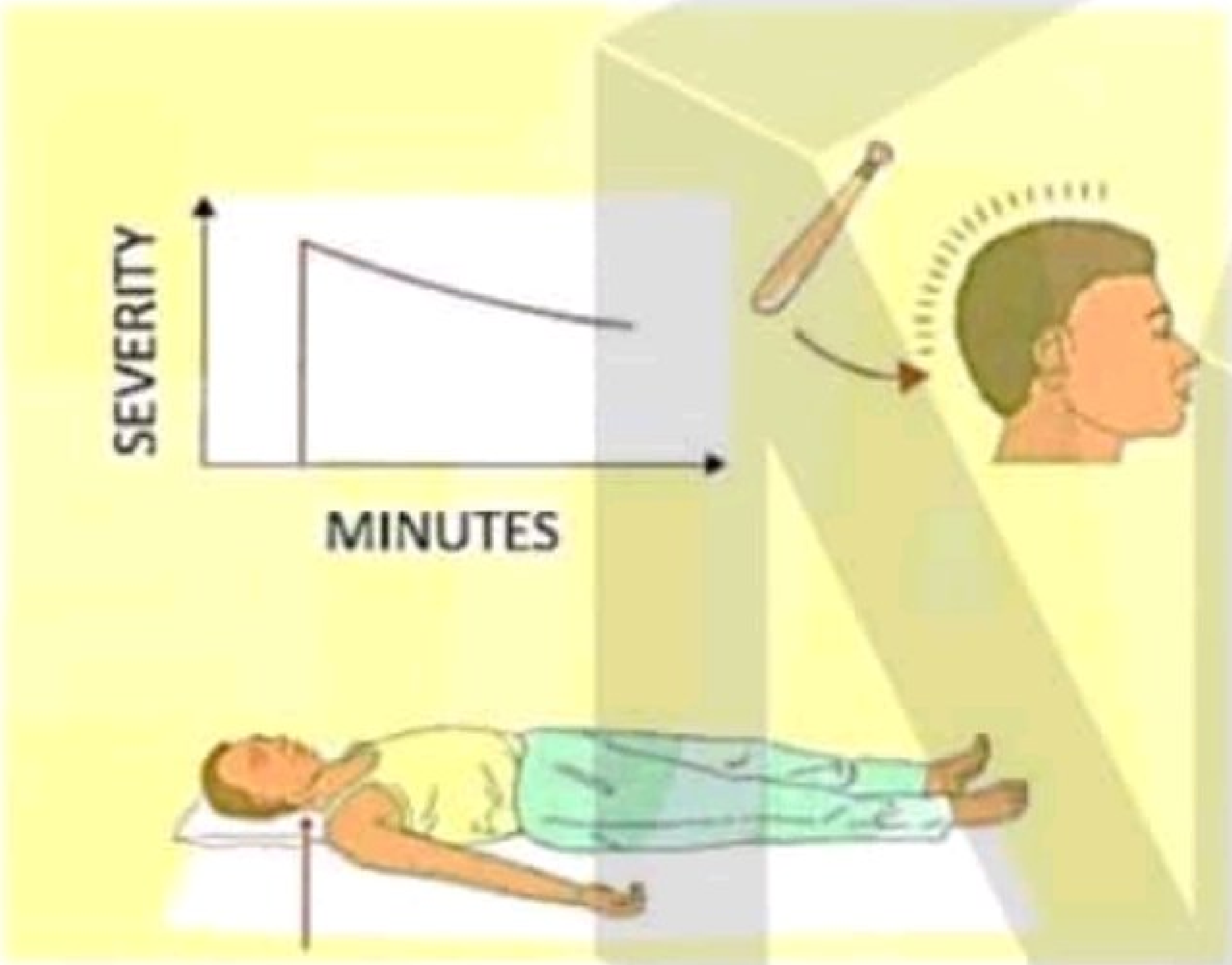


Ring Enhancing lesion with Eccentric 'Target' appearance

Dx: Toxoplasmosis

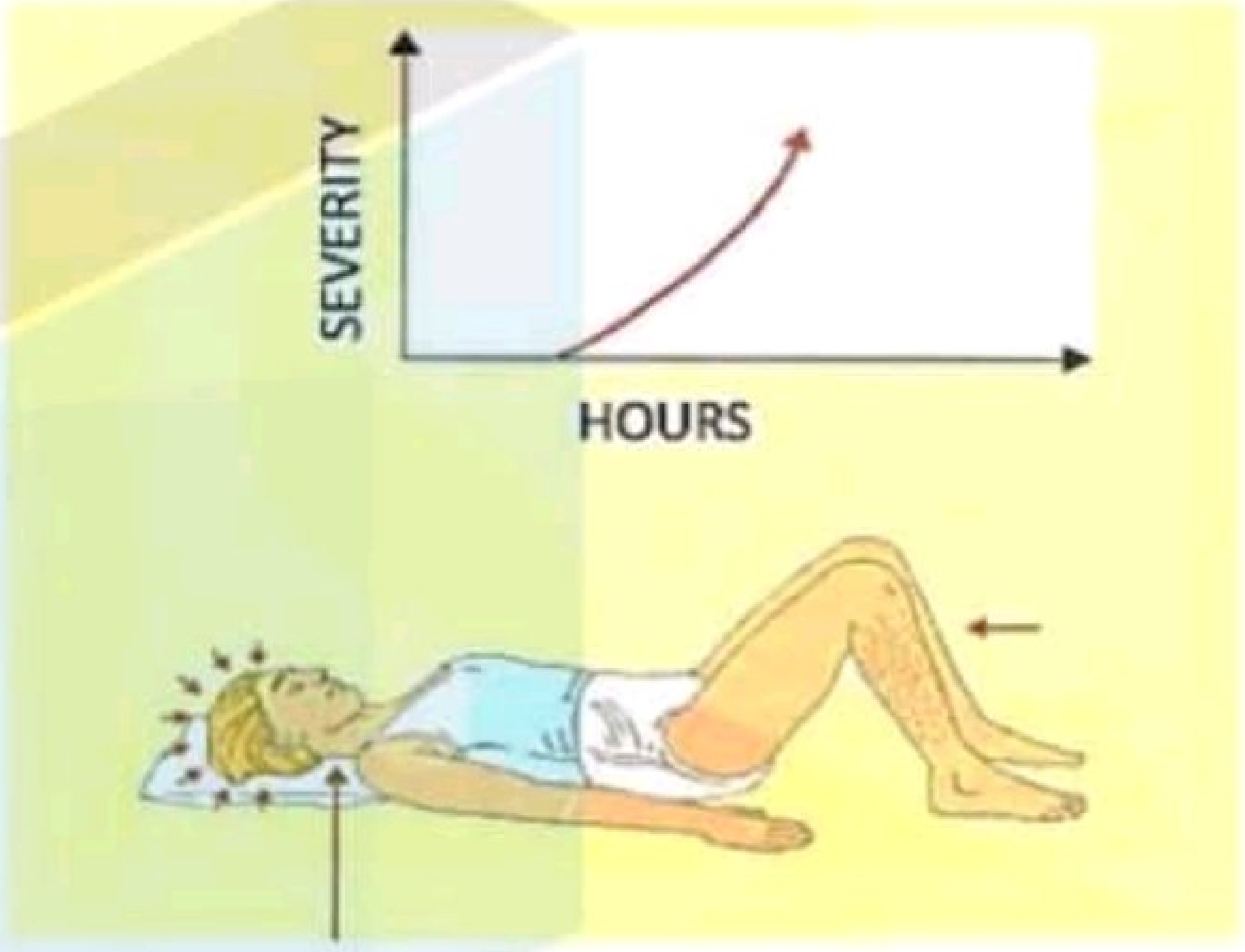
Secondary Headaches

SAH


SEVERITY
MINUTES

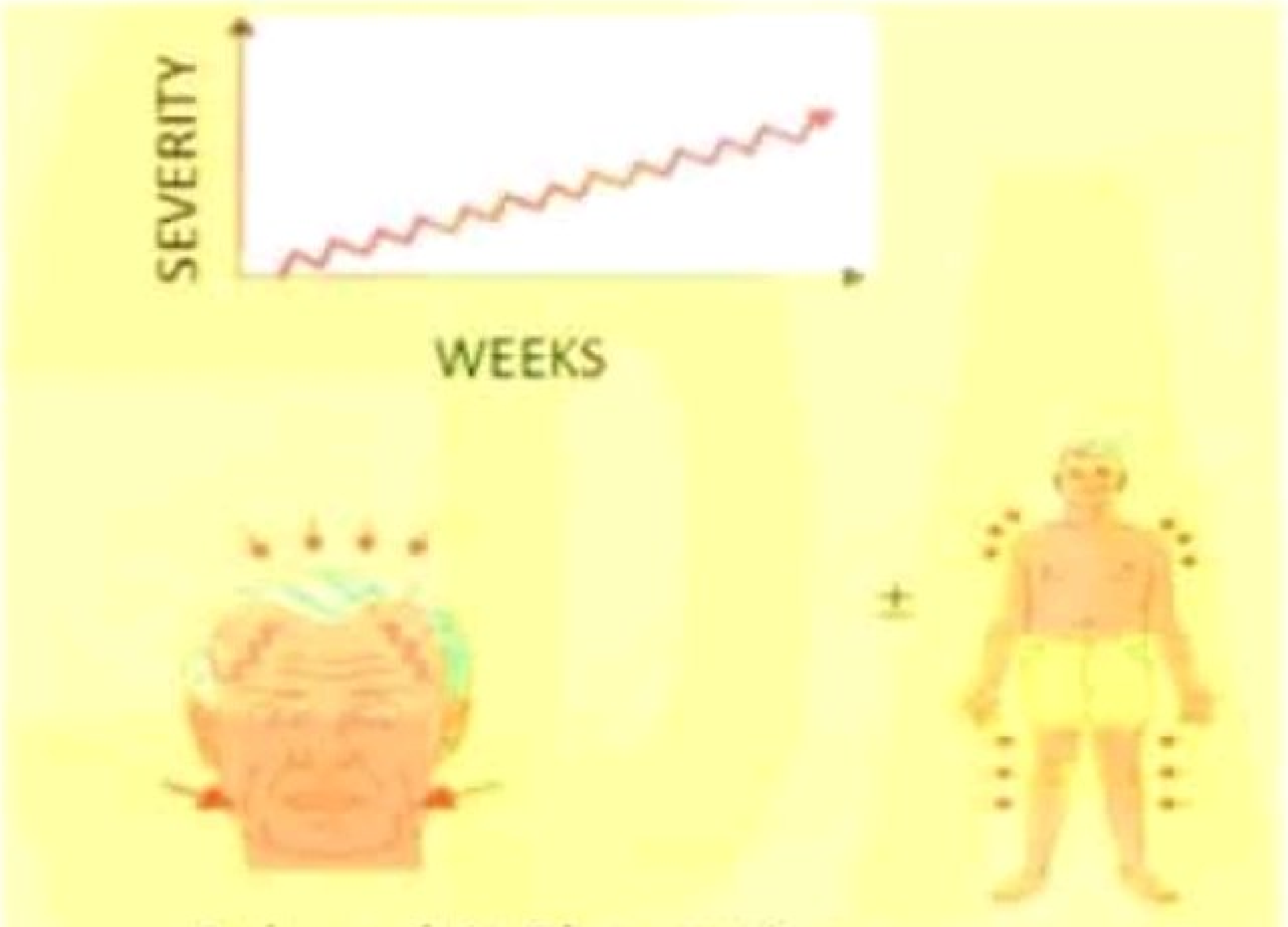
- ✓ THUNDERCLAP HEADACHE
- ✓ NECK STIFFNESS
- ✓ NO FND

MENINGITIS


SEVERITY
HOURS

- ✓ GRADUALLY PROGRESSIVE HEADACHE
- ✓ NECK STIFFNESS
- ✓ FEVER

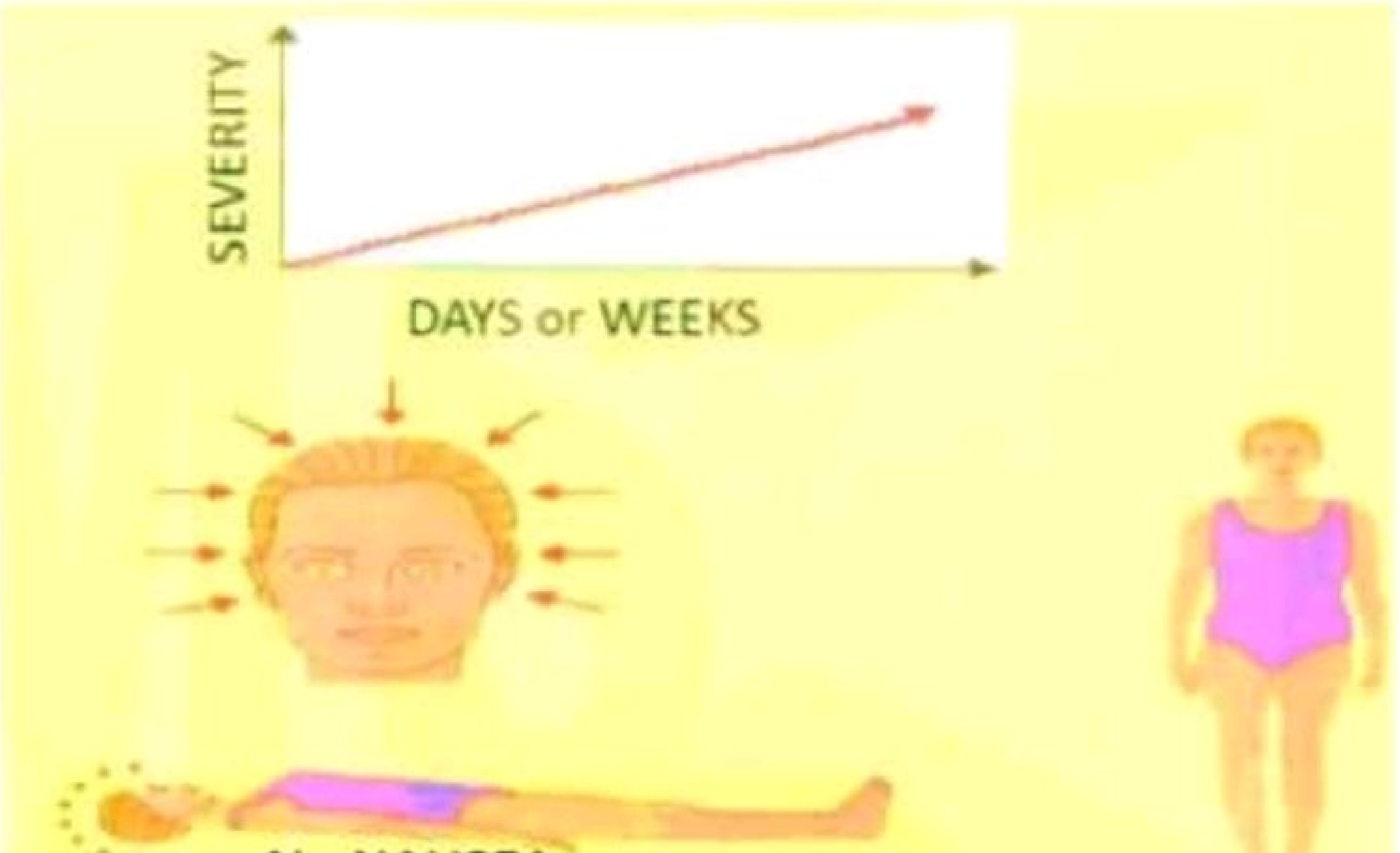
TEMPORAL ARTERITIS


SEVERITY
WEEKS
±

Polymyalgia Rheumatica

- ✓ BITEMPORAL PAIN
- ✓ JAW CLAUDICATION
- ✓ SCALP TENDERNESS
- ✓ MUSCLE ACHES

RAISED ICP


SEVERITY
DAYS or WEEKS

No NAUSEA

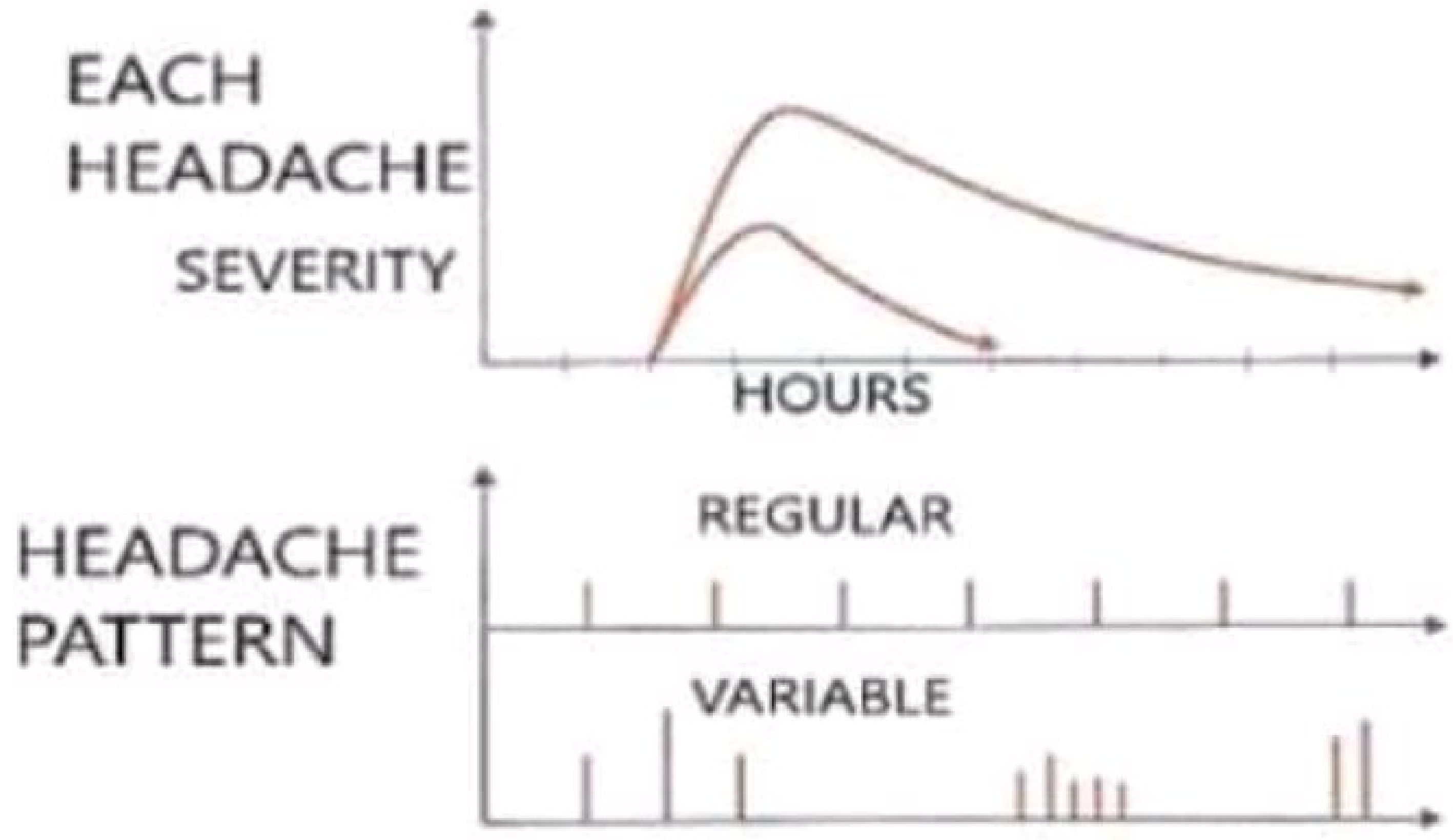
- ✓ GENERALIZED HEADACHE
- ✓ PROJECTILE VOMITING
- ✓ PAPILLEDEMA
- ✓ POSTURAL TRIGGER

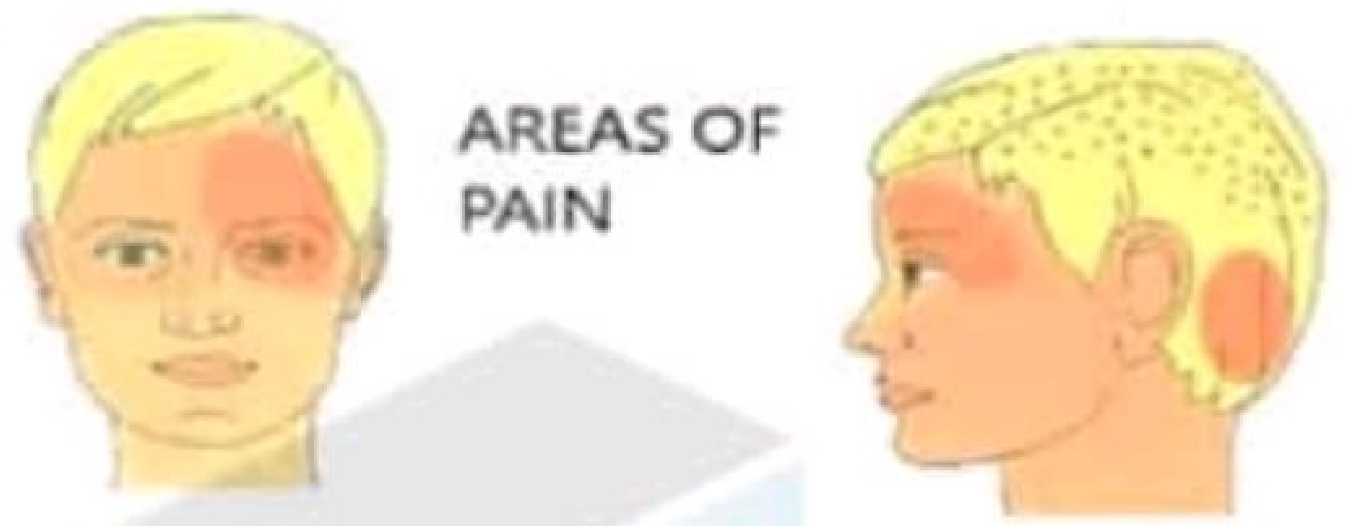
- **Obese female with increased ICP → Think of pseudotumor cerebri**

MIGRAINE

PULSATILE UNILATERAL THROBBING HEADACHE (4-72 HOURS) WITH NAUSEA/VOMITING OR **PHOTO/PHONO PHOBIA**

✓ AURA PRESENT -CLASSICAL MIGRAINE (20%)
✓ AURA ABSENT -COMMON MIGRAINE (80%)
❖ DOC –Triptans
❖ Prophylaxis
✓ Beta blockers
✓ AED
✓ CCB
✓ TCA

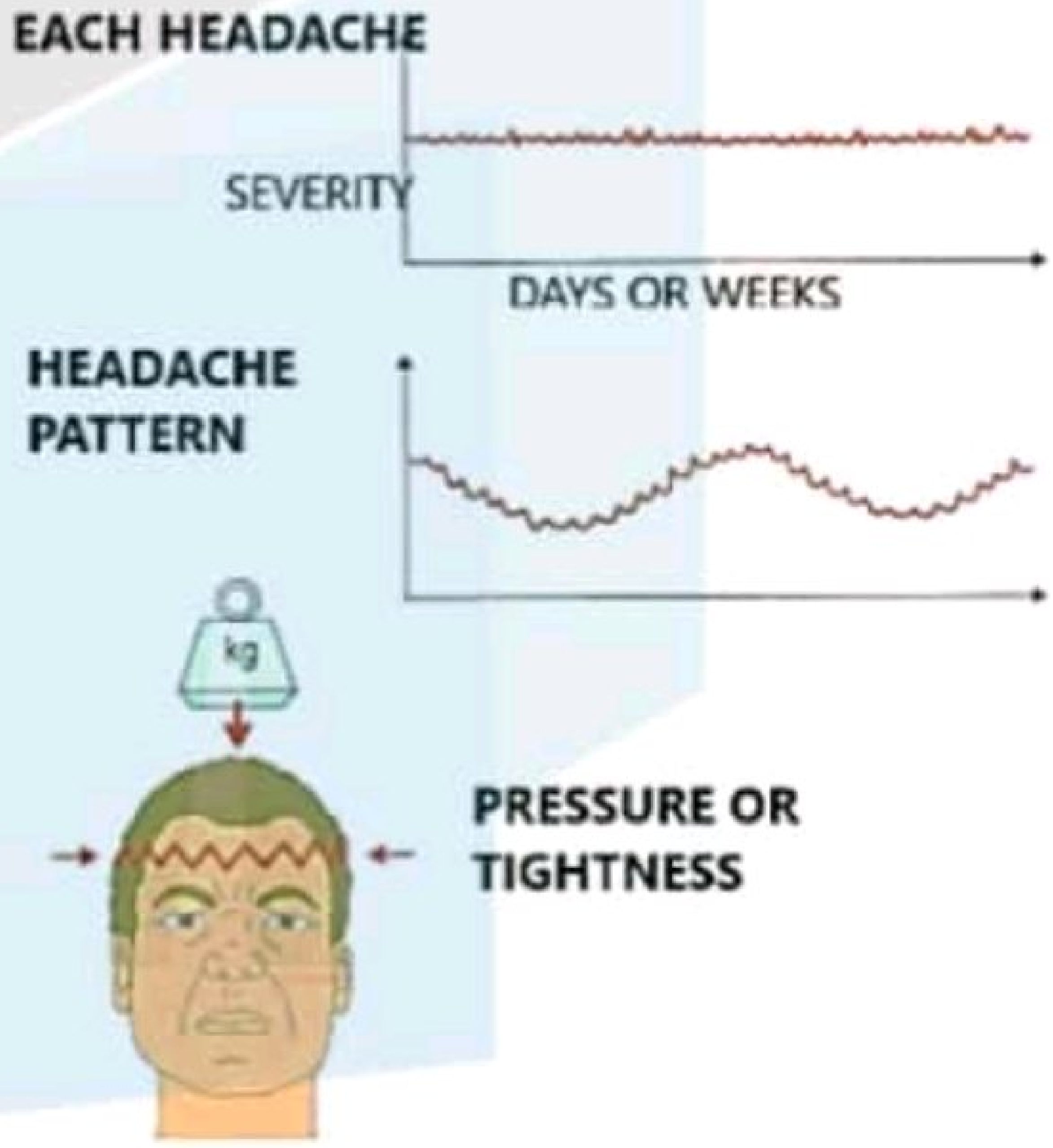




TENSION HEADACHE

✓ DULL ACHING
✓ BAND LIKE SENSATION
✓ ASSOC WITH DEPRESSION

❖ **TOC**
✓ Episodic –Analgesics
✓ Chronic –TCA.



CLUSTER HEADACHE

- **UNILATERAL EXPLOSIVE HEADACHE**
- **15-180 MINUTES**
- **PTOSIS**
- **LACRIMATION**
- **RHINORRHEA**

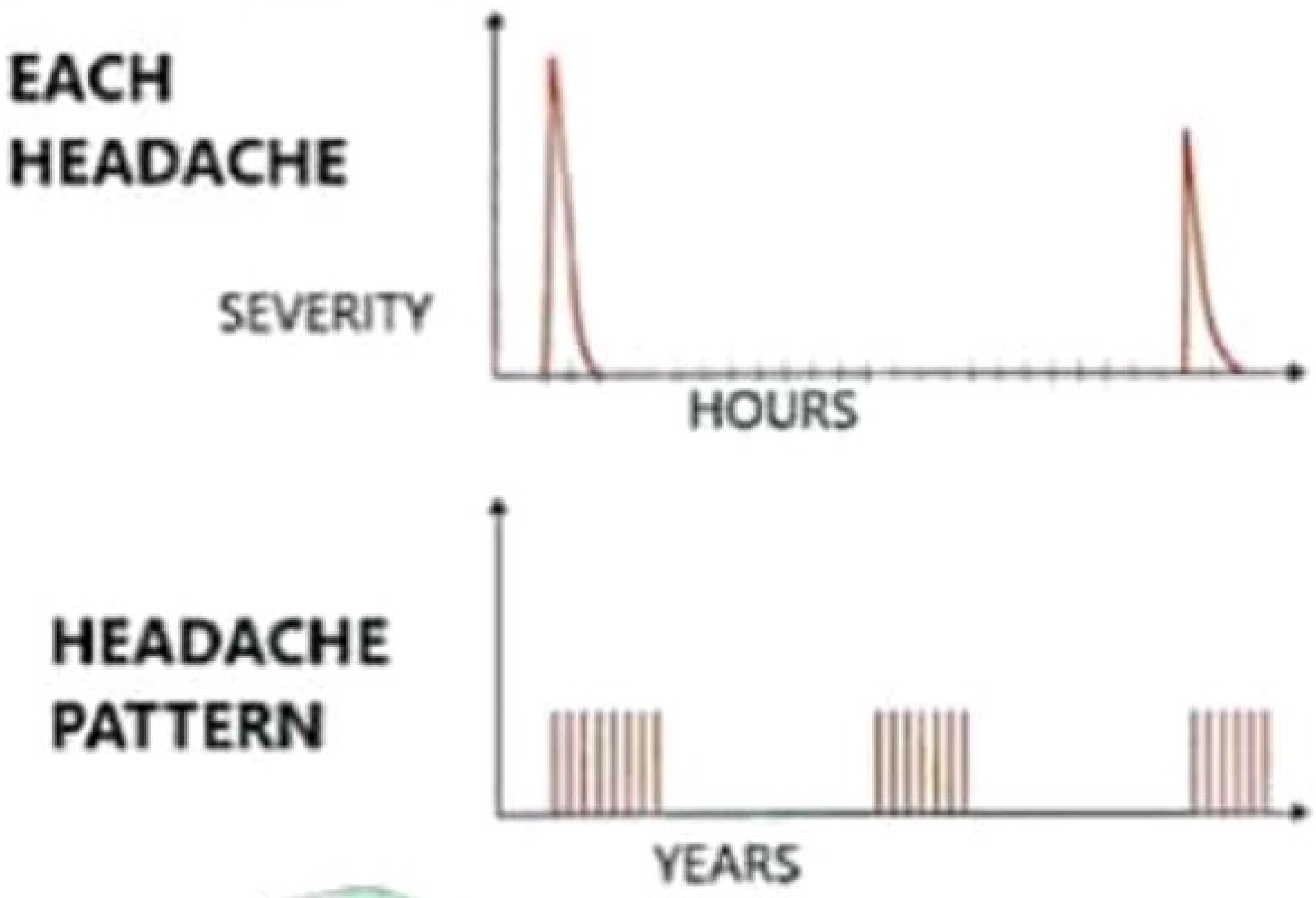
TOC

ACUTE ATTACK

Oxygen inhalation

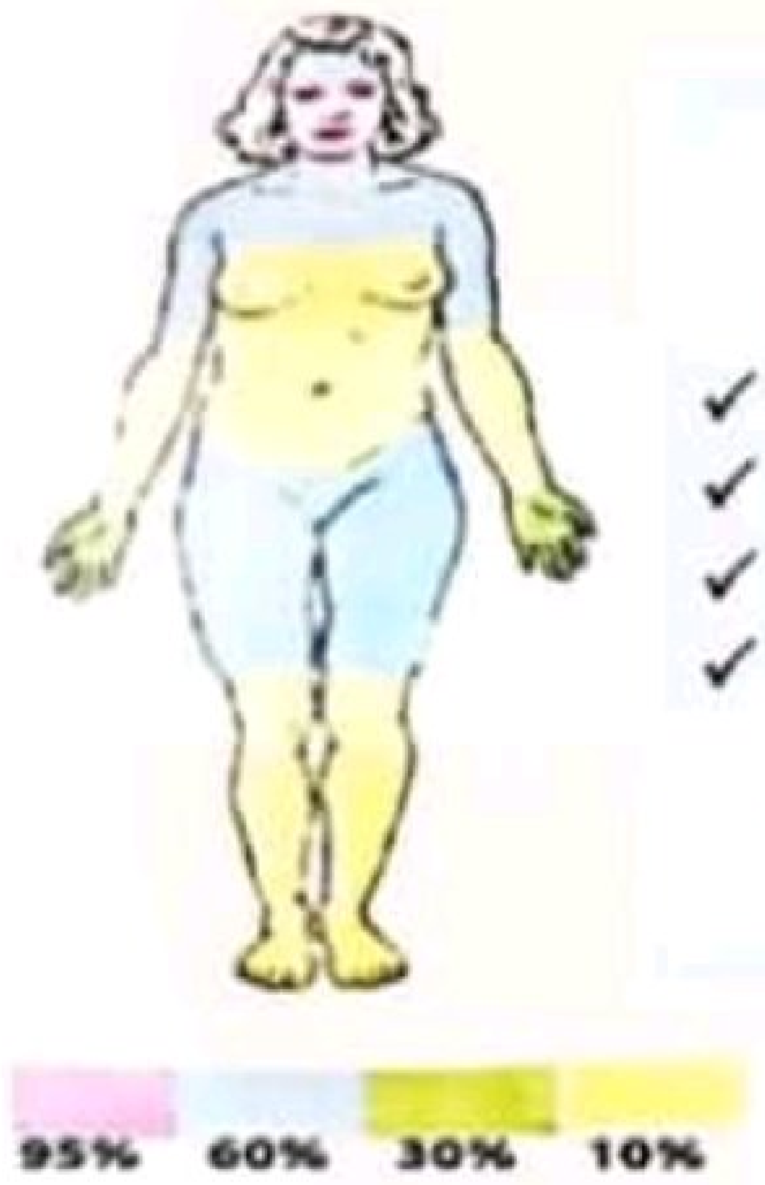
PROPHYLAXIS

VERAPAMIL



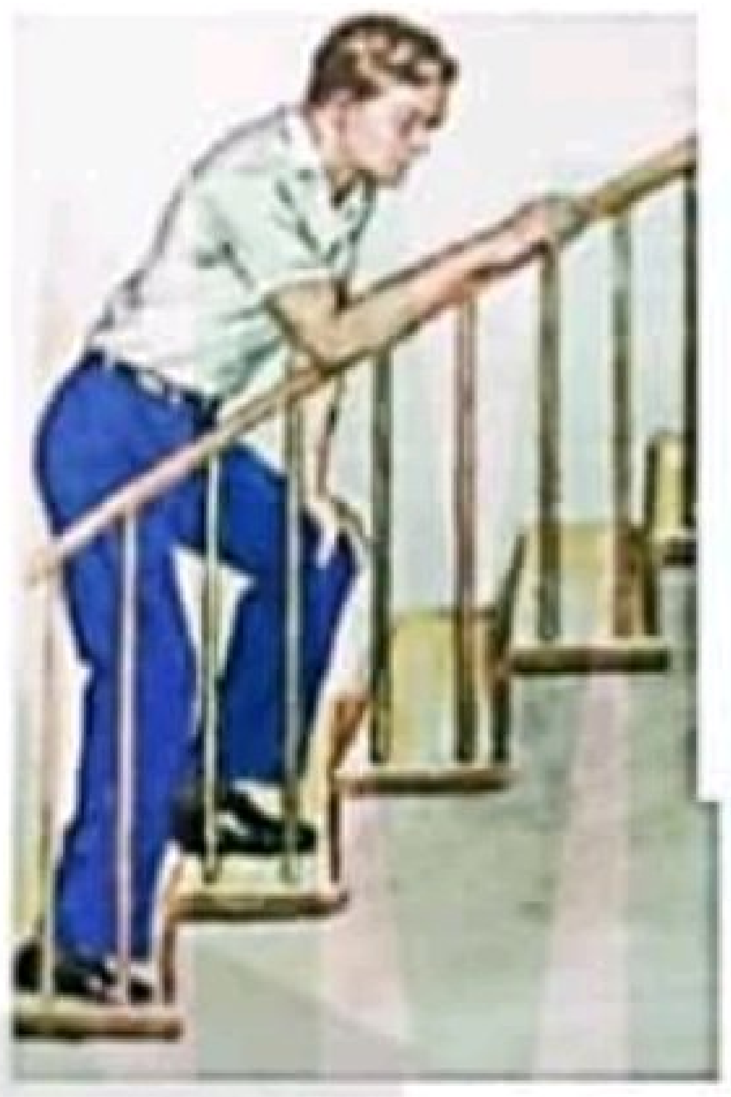
NMJ DISORDERS

MG

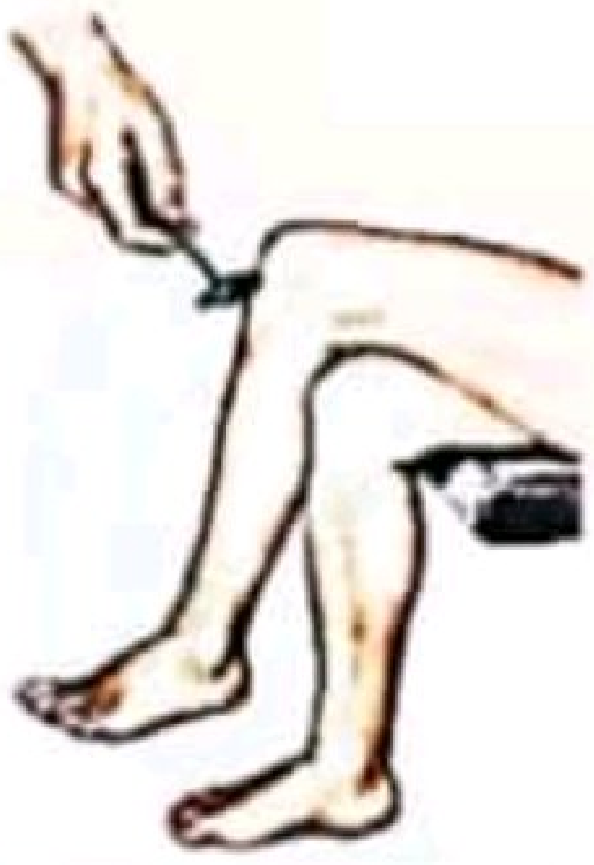


NORMAL
- ✓ SENSORY
- ✓ AUTONOMIC
- ✓ DTR
- ✓ COGNITION

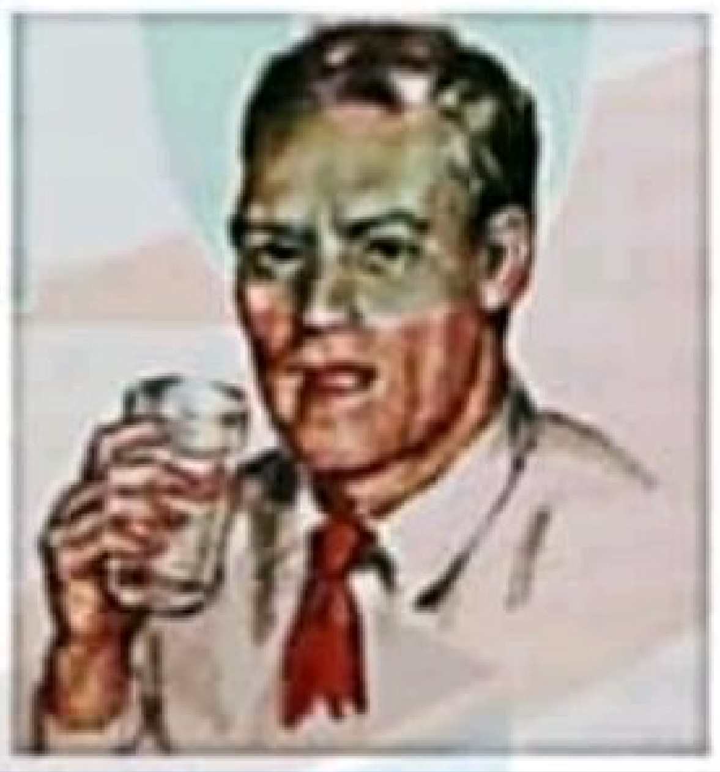
LEMS



EARLY SKELETAL MUSCLE WEAKNESS



AREFLEXIA



AUTONOMIC INVOLVEMENT – DRYNESS OF MOUTH

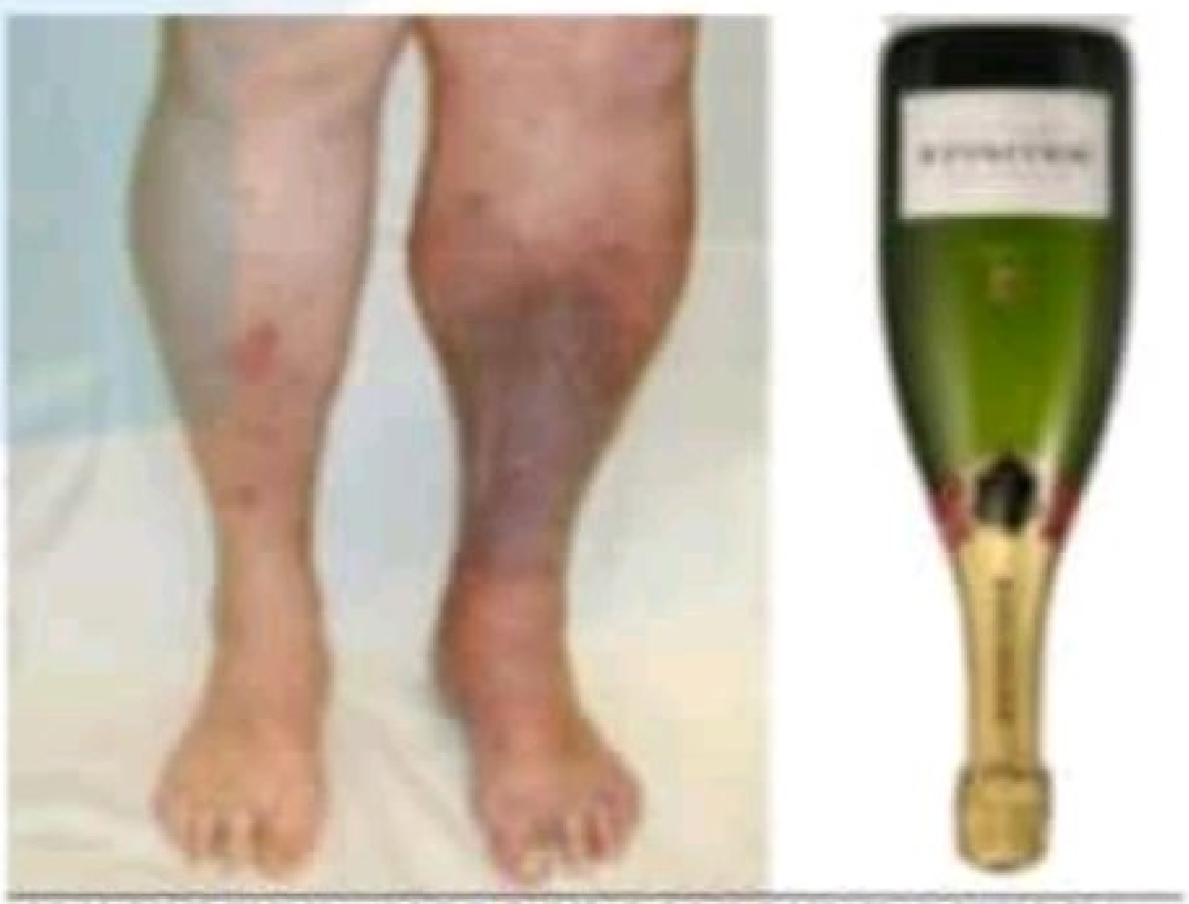
	MG	LEMS
Associated with	THYMIC –Hyperplasia (65%) Thymoma (10 %)	SCC Lung
EDROPHONIUM TEST	+++++	+/-
ACHR abs	Positive MOST SPECIFIC TEST GOLD STANDARD TEST	Negative
RAPID NERVE STIMULATION	Decremental response	Decremental @low frequency Incremental high frequency
SFEMG	JITTER Advised only if AchR abs negative	-
TREATMENT	PYRIDOSTIGMINE (DOC) IMMUNOSUPRESSANTS THYMECTOMY	3,DAP Amifampridine

POST INFECTIOUS DEMYELINATING POLYNEUROPATHY

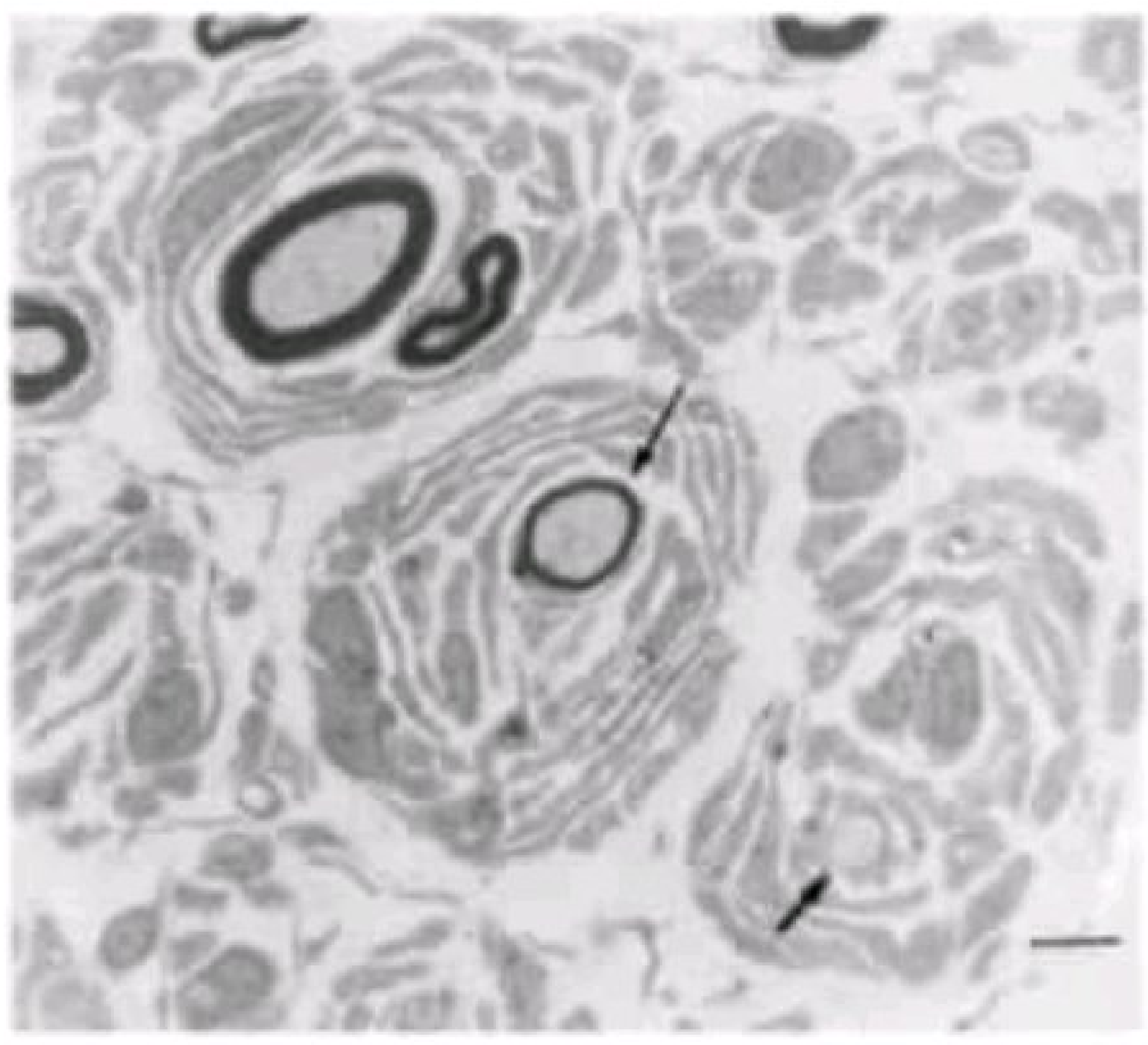
	AIDP	CIDP
DEFINITION	MONOPHASIC B/L SYMMETRICAL ASCENDING PARALYSIS WITH MAX WEAKNESS IN 28 DAYS	Weakness deteriorates >9 weeks of onset or relapses at least three times
NERVE involvement	MOTOR>SENSORY	MOTOR/SENSORY SYMM INVOLVEMENT ASYMM in multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy variant (Lewis-Sumner syndrome)
TREMORS	-	+ in 10 %
CSF	ACD +	ACD +
NERVE BIOPSY	DEMYELINATION	ONION BULB APPERANCE
NERVE CONDUCTION STUDY	CONDUCTION BLOCKS DEC.NCV	CONDUCTION BLOCKS DEC.NCV
TREATEMENT	i.v Ig /Plasmapheresis	i.V Ig/Plasmapheresis
STEROIDS	NO ROLE	Can be used

CHARCOT MARIE TOOTH DISEASE

- CMT type 1, 2, 3 – Autosomal Dominant
- CMT type 4 – Autosomal Recessive
- CMT Type 1 is the M/C type
- Onset at 1st to 3rd decade
- Foot Drop- M/C presentation
- DTR decreased/absent, sensation is lost
- Motor NCV- 20-25/sec
- Nerve biopsy→ Onion Bulb



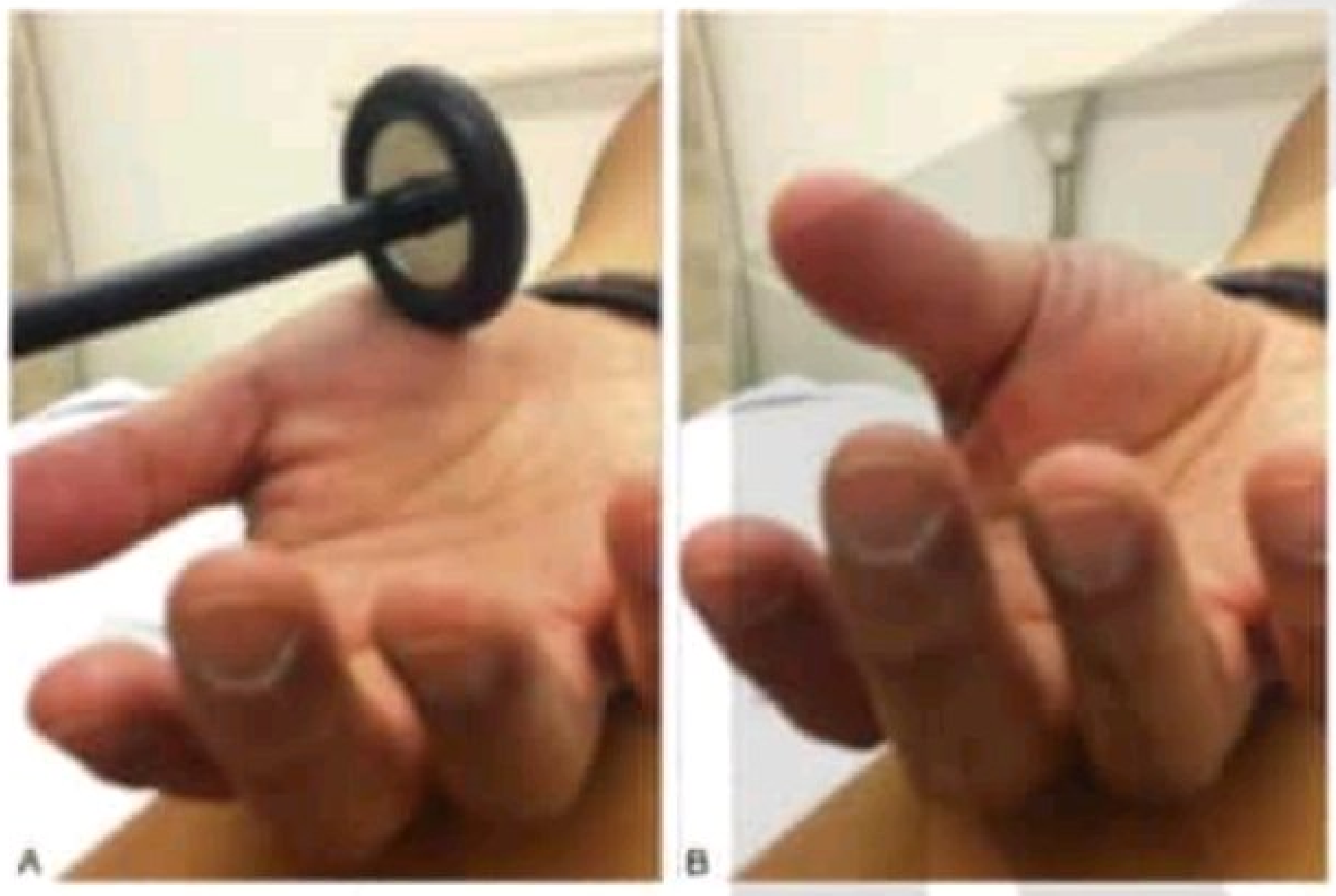
INVERTED CHAMPANGNE BOTTLE APPEARANCE

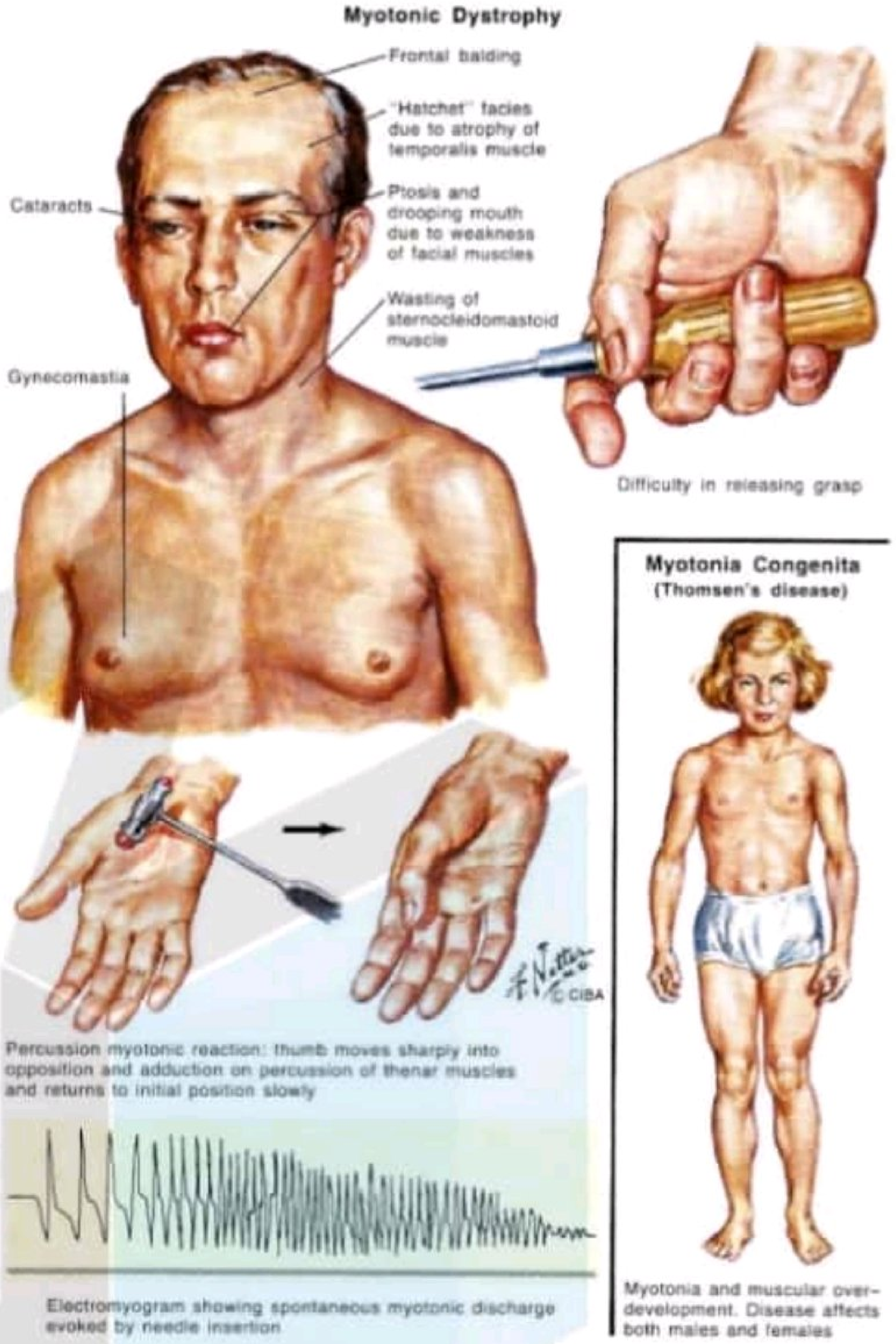


Myotonic Dystrophy

- M/C Adult Muscular Dystrophy
- Autosomal Dominant
- CTG sequence defect on Chromosome 19
- Myotonia: Delayed release on an object which is gripped once
- Percussion Myotonia: Sudden contraction of hand muscles when thenar muscles are percussed.

- Rx: MEXILITINE




Myotonic Dystrophy
Frontal balding
"Hatchet" facies due to atrophy of temporalis muscle
Cataracts
Ptosis and drooping mouth due to weakness of facial muscles
Wasting of sternocleidomastoid muscle
Gynecomastia
Difficulty in releasing grasp
Myotonia Congenita (Thomsen's disease)
F. Netter
© CIBA

Percussion myotonic reaction: thumb moves sharply into opposition and adduction on percussion of thenar muscles and returns to initial position slowly

Electromyogram showing spontaneous myotonic discharge evoked by needle insertion

Myotonia and muscular overdevelopment. Disease affects both males and females

Brain Tumours

Popular One liners:

- M/C Brain tumours overall: **METASTASIS** > Glioma> Meningioma > Astrocytoma

- M/C primary for brain secondaries: **Lungs** (commonly- Small cell lung Cancer)

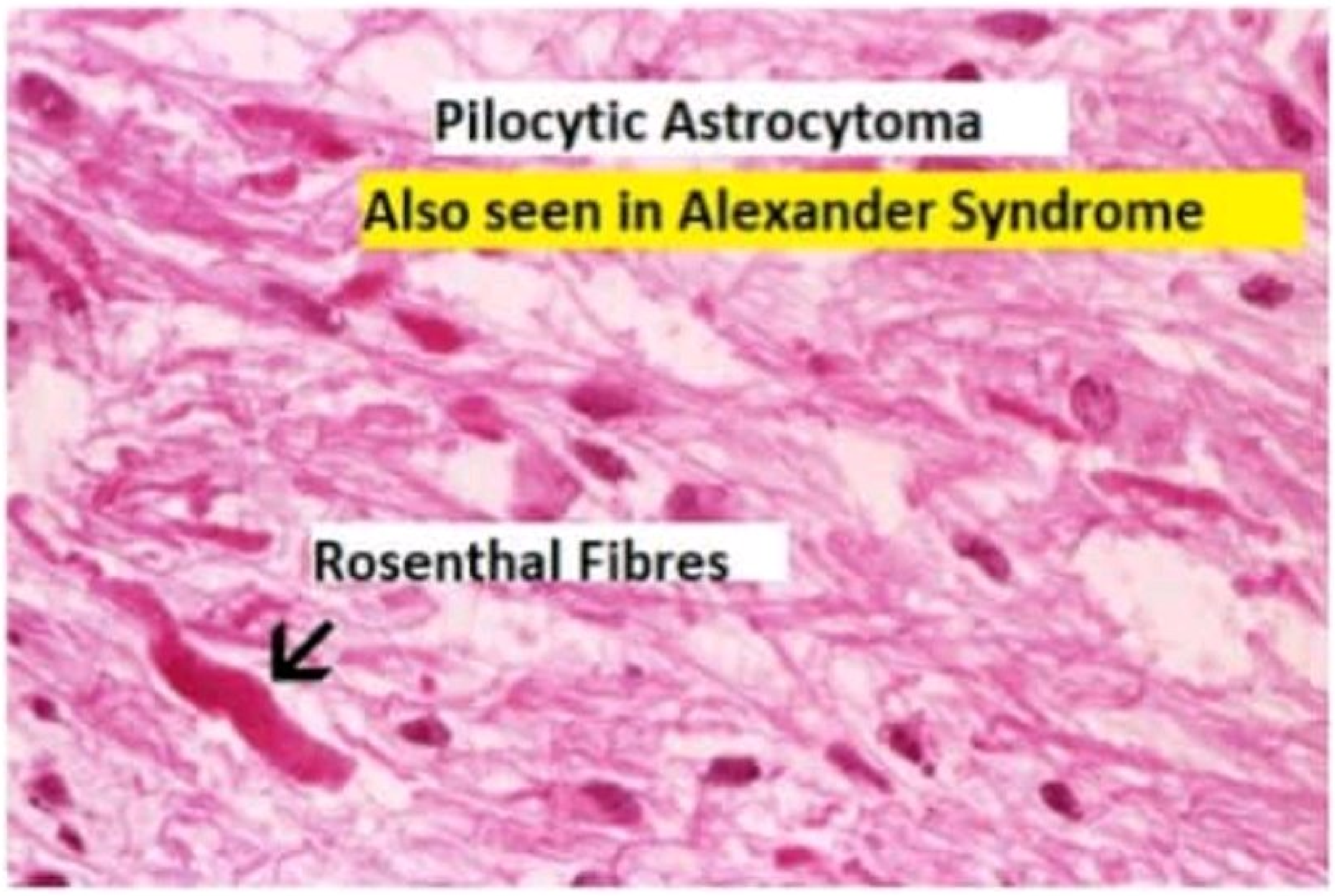
- M/C Primary malignant tumour (Overall/Adults): **Glioblastoma**

- M/C tumour in children: **Pilocytic Astrocytoma** (Supratentorial location)

- M/C malignancy of brain in children: **Medulloblastoma** (Infratentorial)

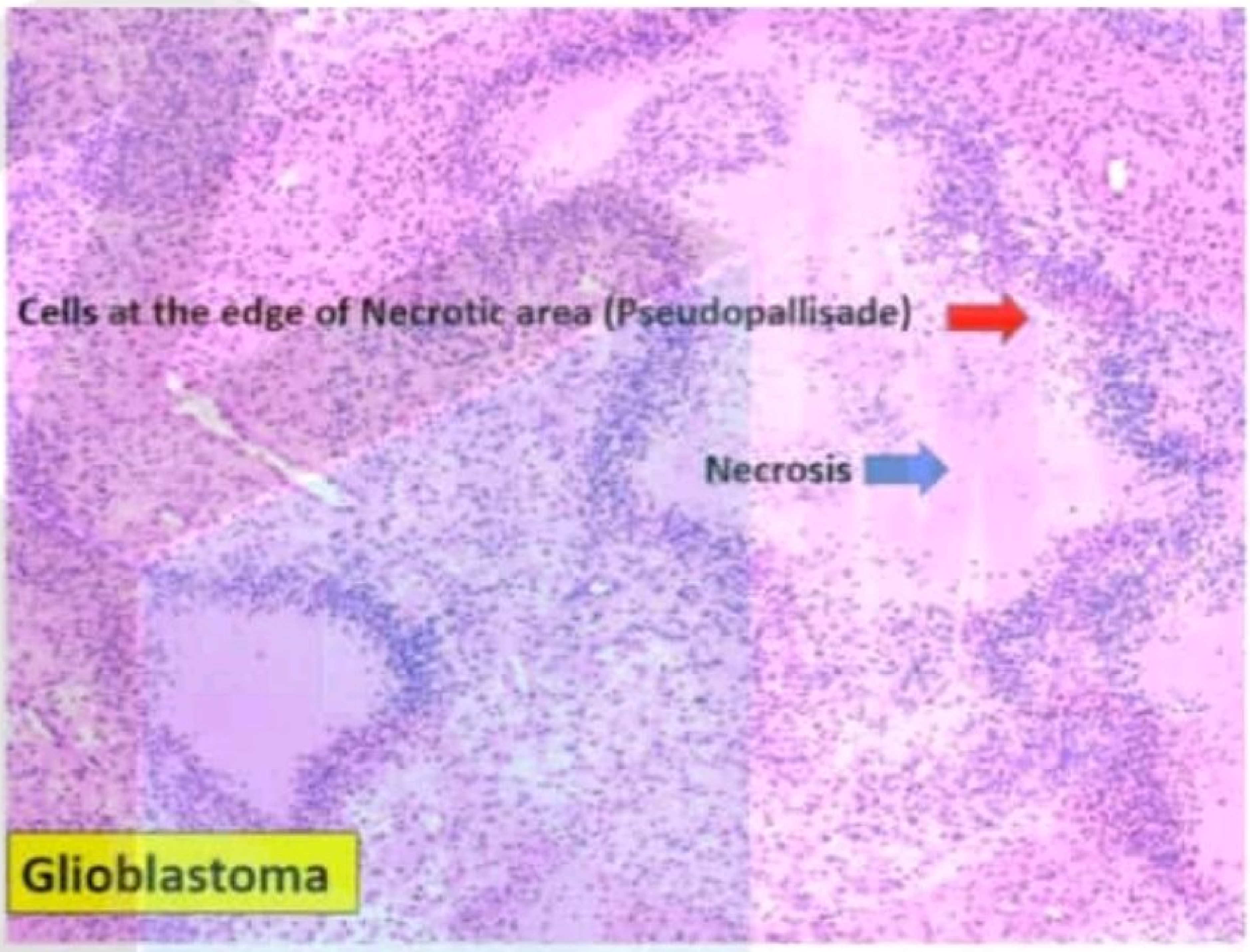
Brain Tumors (Histopath)

1. Pilocytic Astrocytoma


Pilocytic Astrocytoma
Also seen in Alexander Syndrome
Rosenthal Fibres

- AKA Optic Nerve Glioma
- Clinical: 8-year-old child with progressive loss of vision, but no complete blindness.
- HPE: Rosenthal Fibres
- Benign Tumour (Grade 1)

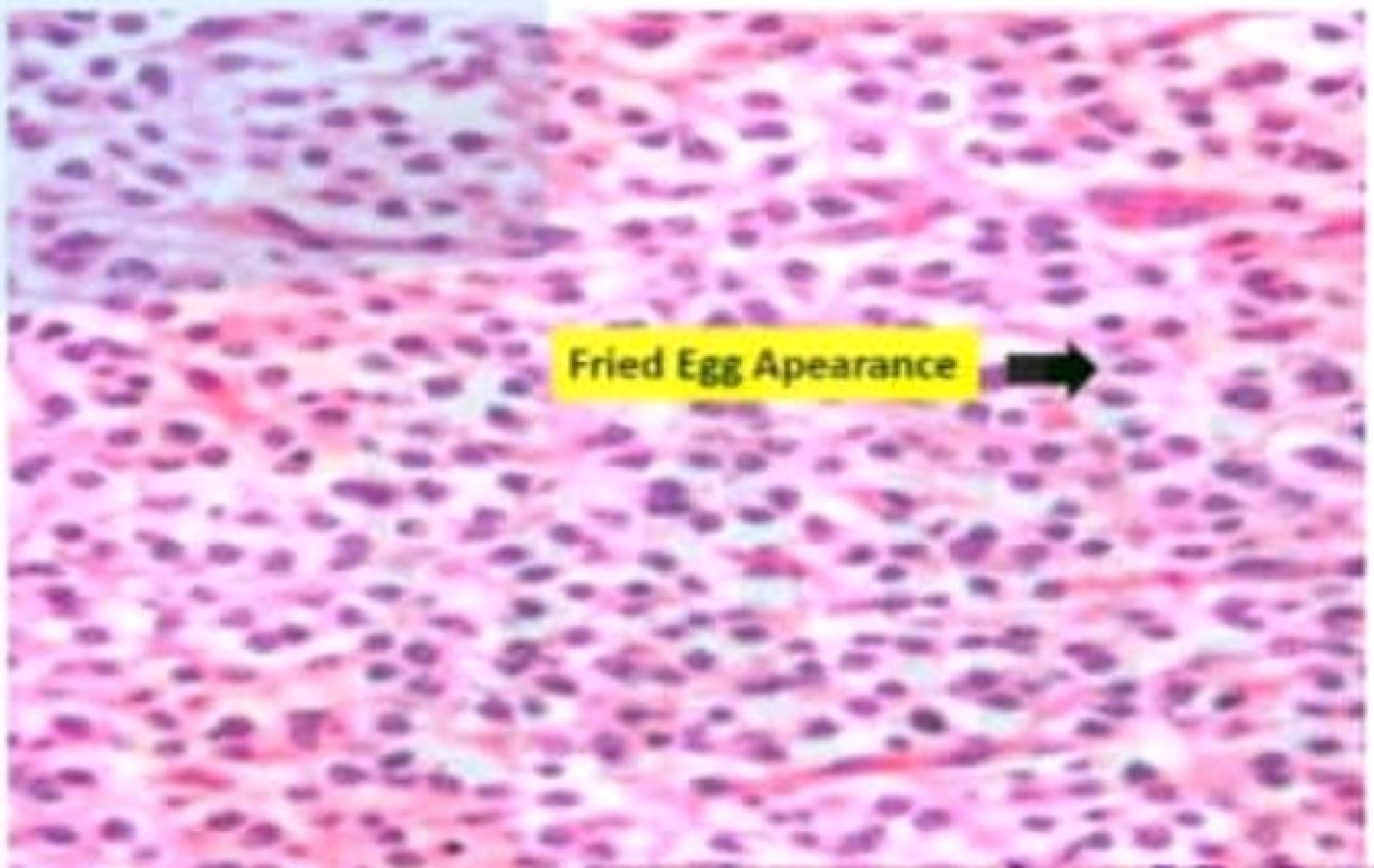
2. Glioblastoma

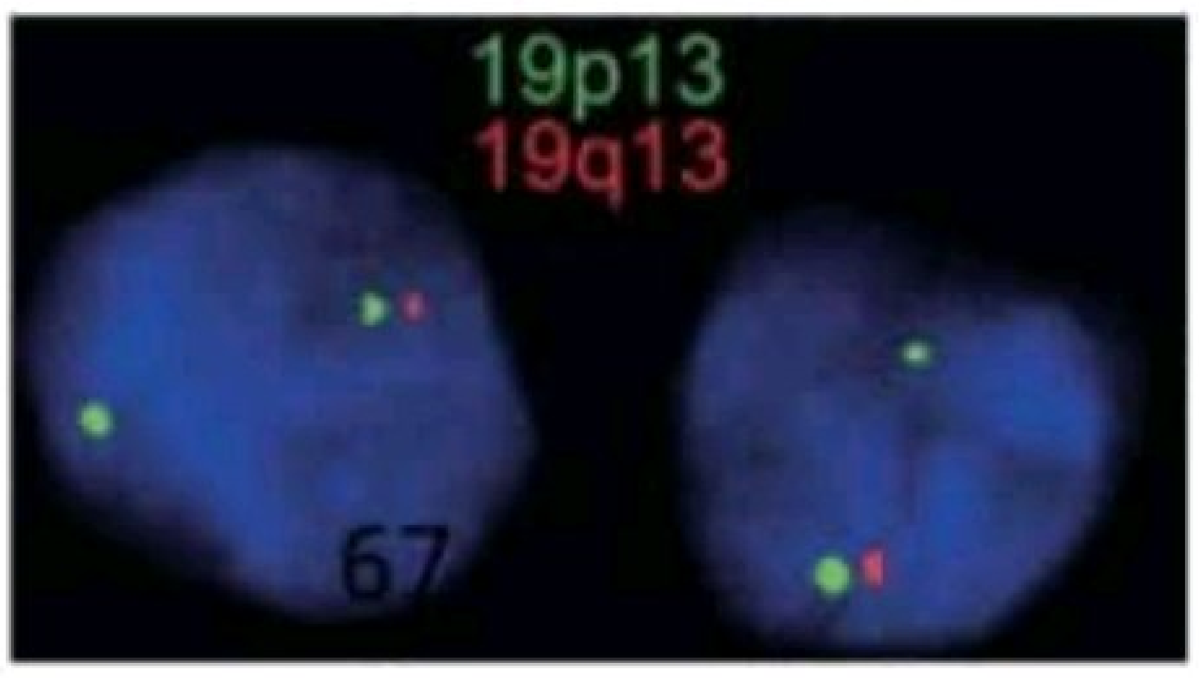

Cells at the edge of Necrotic area (Pseudopallisade)
Necrosis
Glioblastoma

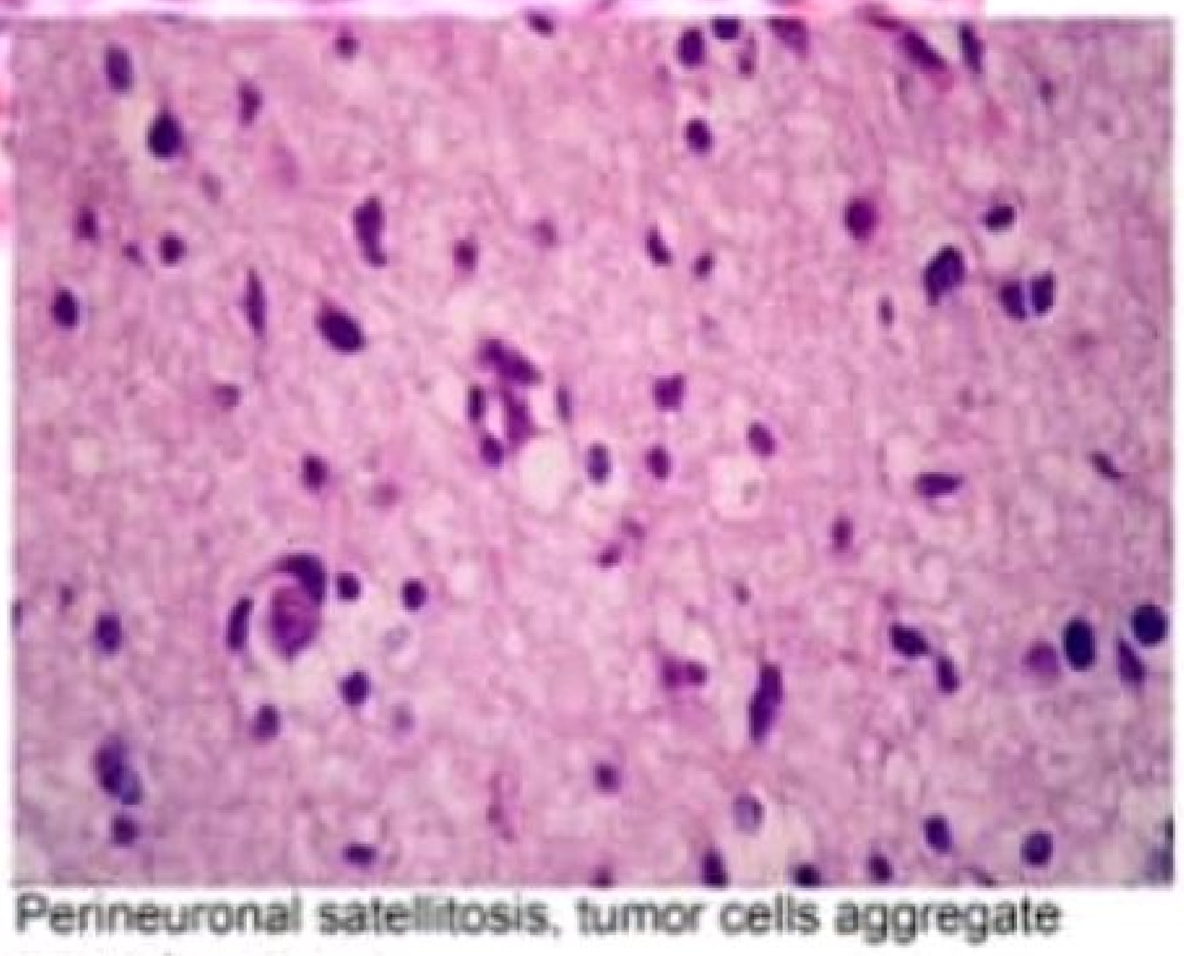
- Clinical: Adult with sudden onset seizures, headache and rapid course of the disease.
- Necrosis indicates the tumour to be high-grade.
- HPE: Necrosis with pseudo-palisading cells at the periphery of the necrosis

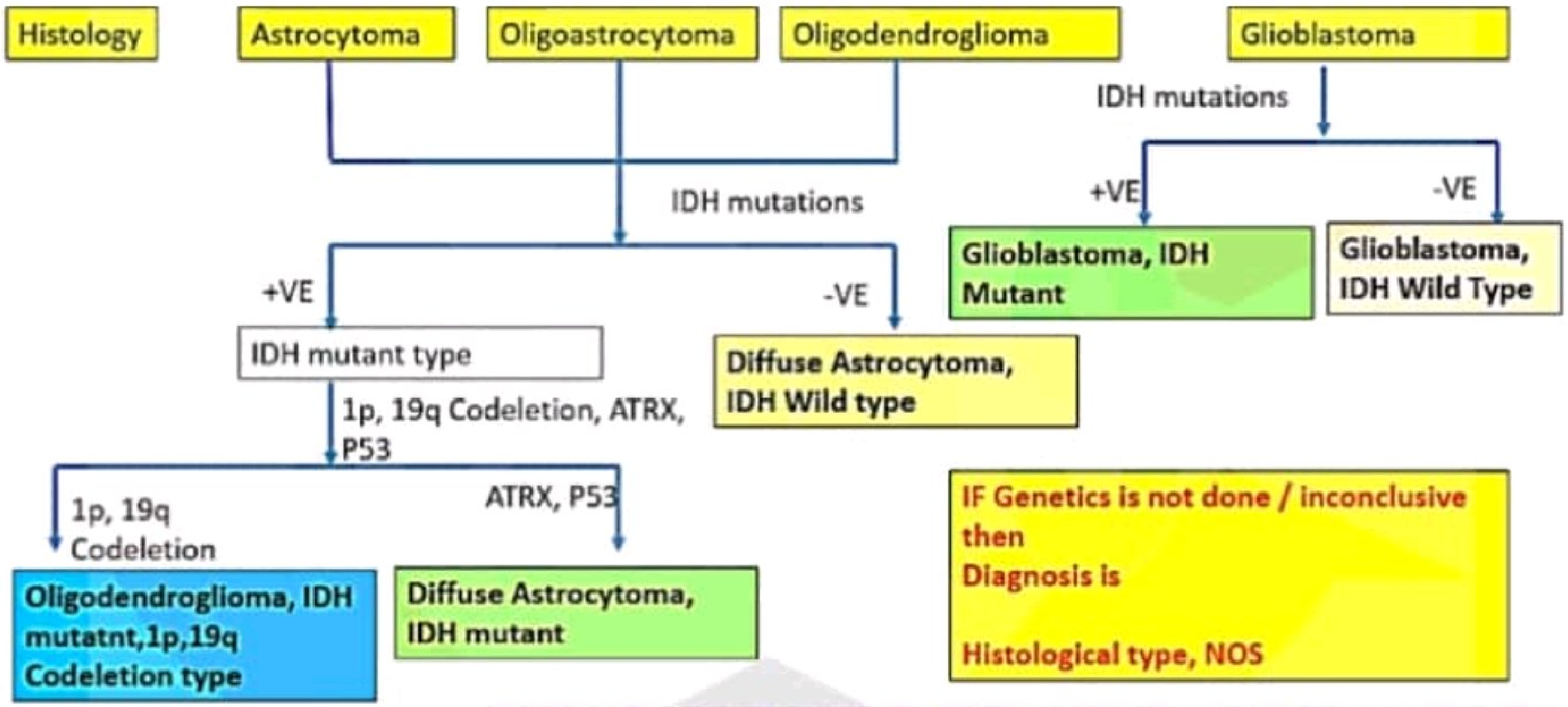
3. Oligodendro Glioma

- Middle aged adult with progressive seizures.
- HPE: Fried Egg Appearance with chicken - wire capillaries and microcalcifications.
- HPE can also show **perineuronal satellitosis**
- Radiology: Calcification


Fried Egg Apearance
Oligodendro Glioma

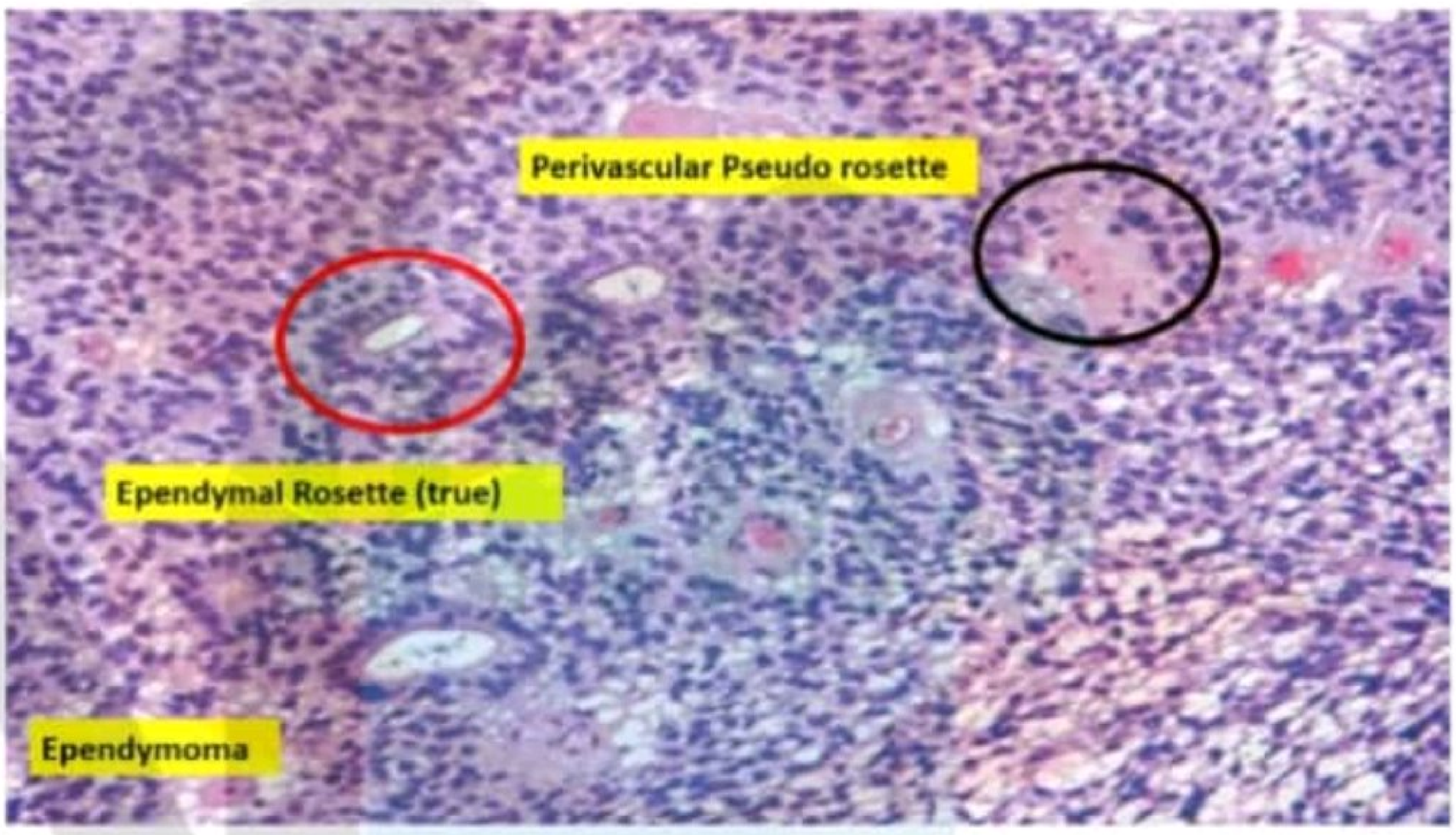

19p13
19q13


Perineuronal satellitosis, tumor cells aggregate around neurons


Histology
Astrocytoma
Oligoastrocytoma
Oligodendroglioma
Glioblastoma
IDH mutations
+VE
-VE
Glioblastoma, IDH Mutant
Glioblastoma, IDH Wild Type
IDH mutations
+VE
-VE
IDH mutant type
Diffuse Astrocytoma, IDH Wild type
1p, 19q Codeletion, ATRX, P53
1p, 19q Codeletion
ATRX, P53
Oligodendroglioma, IDH mutatnt,1p,19q Codeletion type
Diffuse Astrocytoma, IDH mutant
IF Genetics is not done / inconclusive then
Diagnosis is
Histological type, NOS

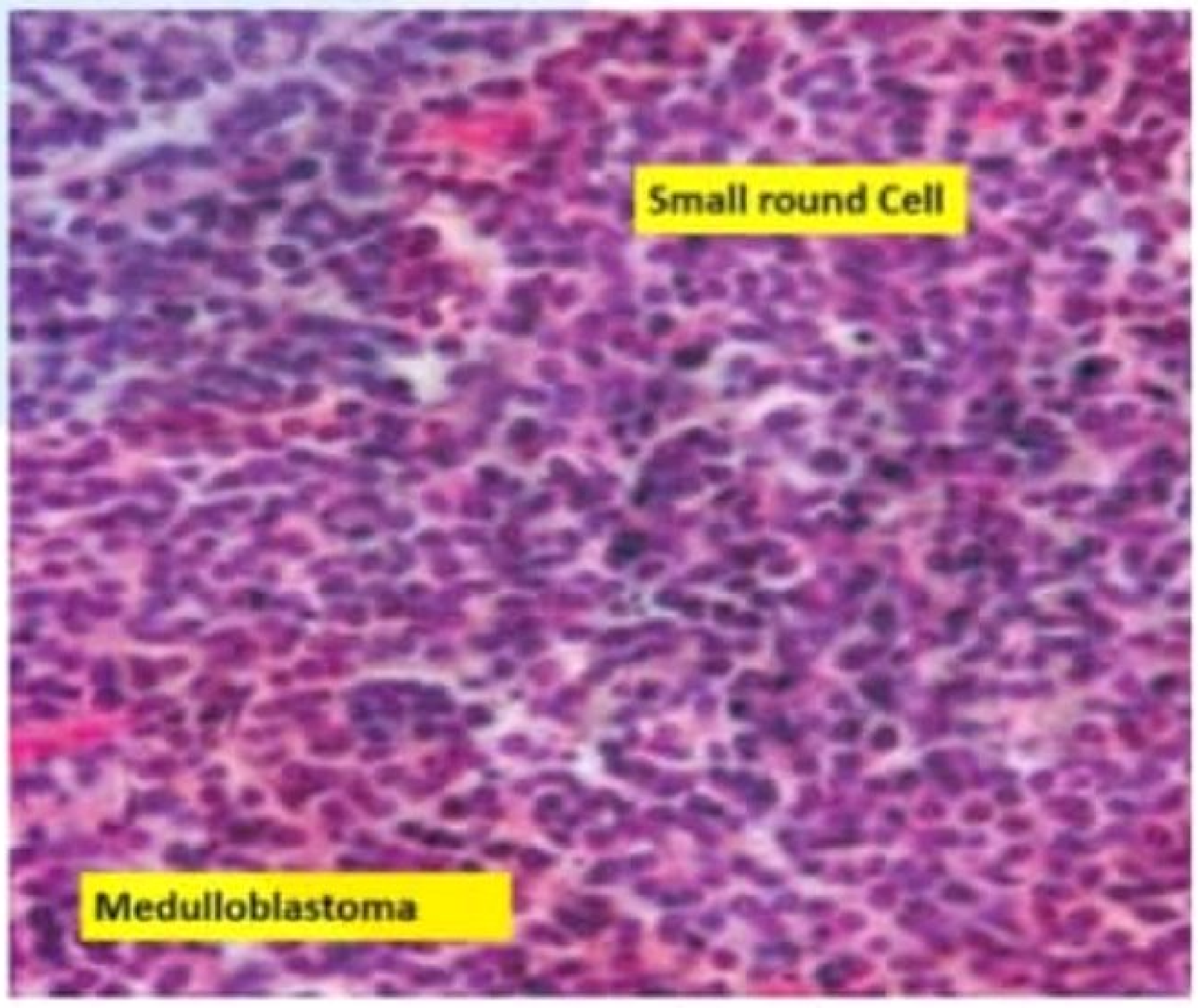
4. Ependymoma

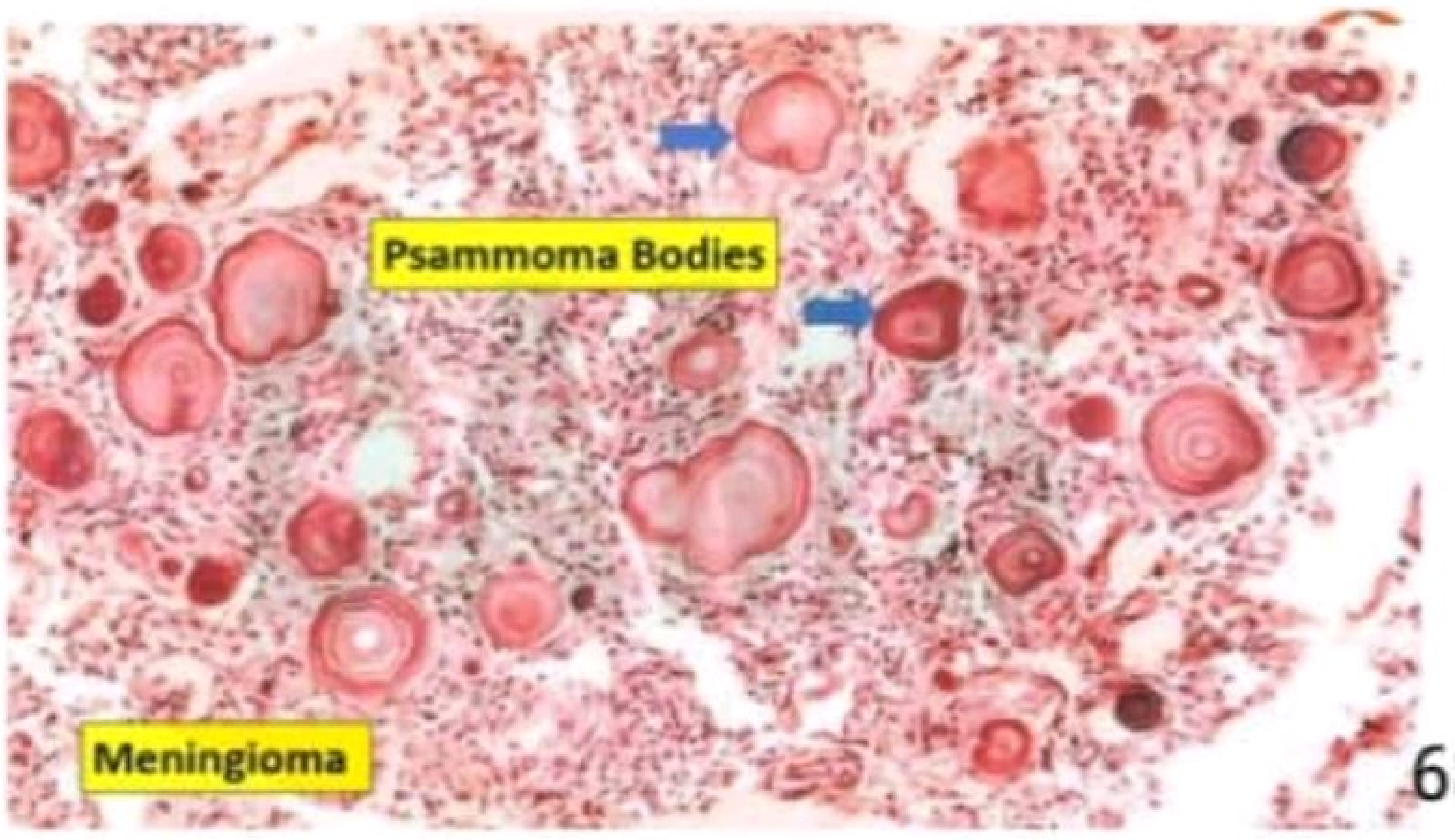
- Perivascular Pseudo-rosettes: Because the centre of the rosette is that of a capillary and not cytoplasm
- Ependymal Rosette: No blood vessel therefore a true rosette.


Perivascular Pseudo rosette
Ependymal Rosette (true)
Ependymoma

5. Medulloblastoma

- Clinically: Child with infratentorial mass.
- HPE: Small round cells.

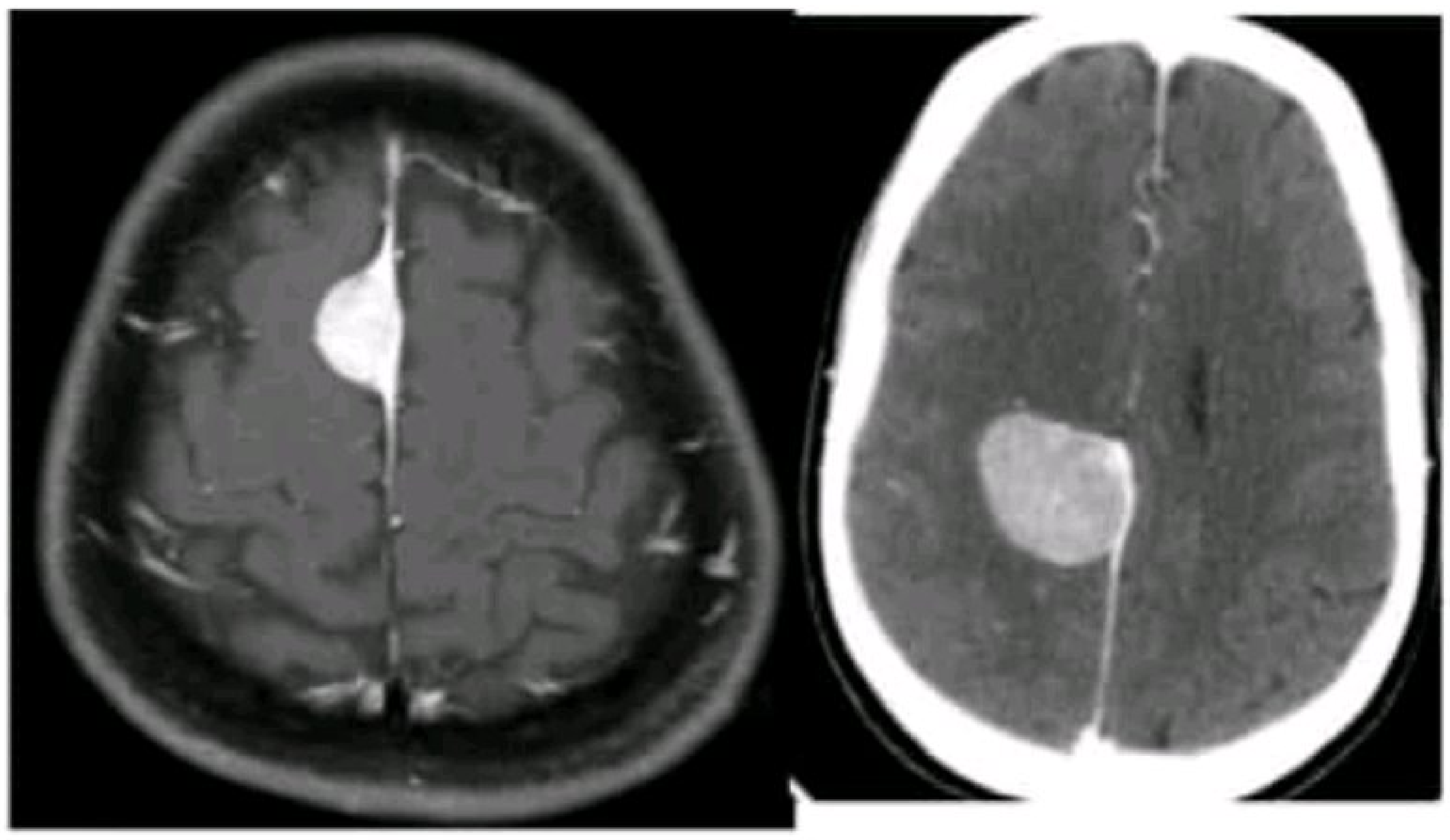

Small round Cell
Medulloblastoma


Psammoma Bodies
Meningioma

6. Meningioma

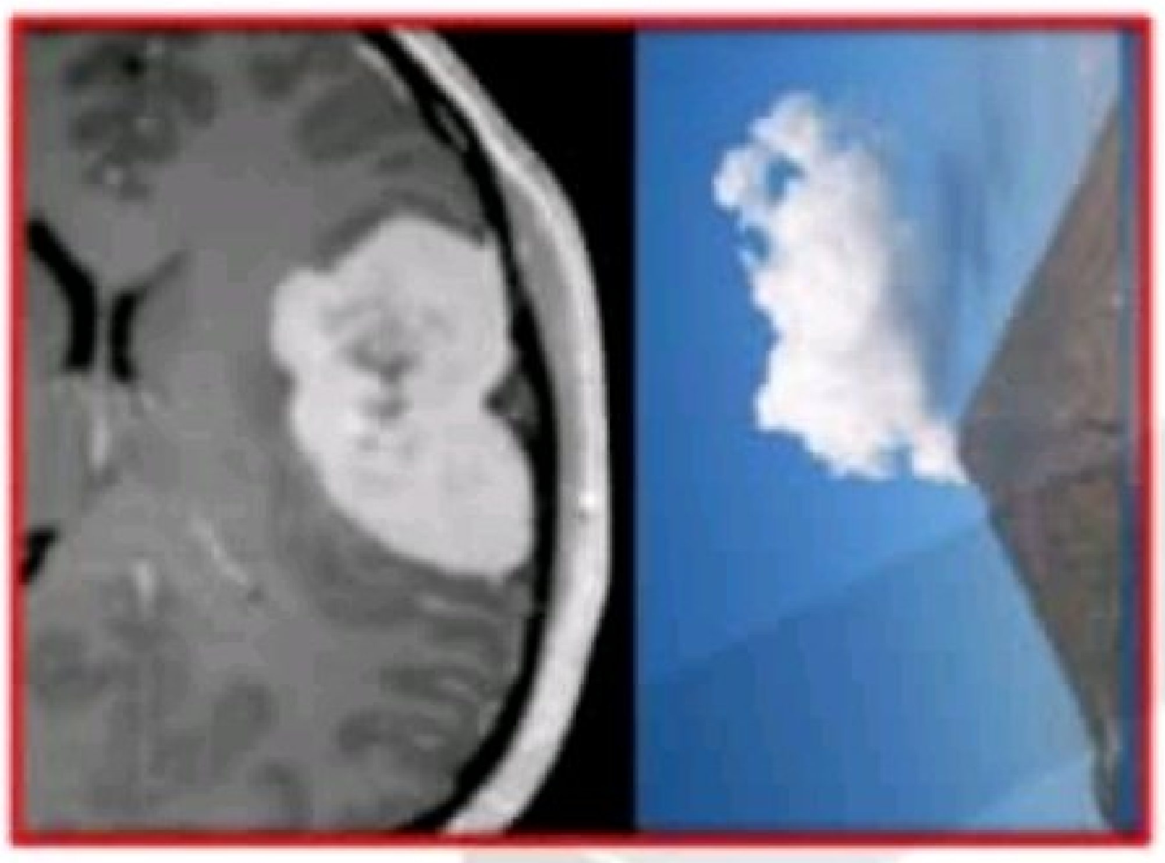
- 35-year-old, multiparous women presenting with headache. (PR +ve)
- HPE: Psammoma Bodies (Lamellated calcium)

Brain Tumours (Radiology)

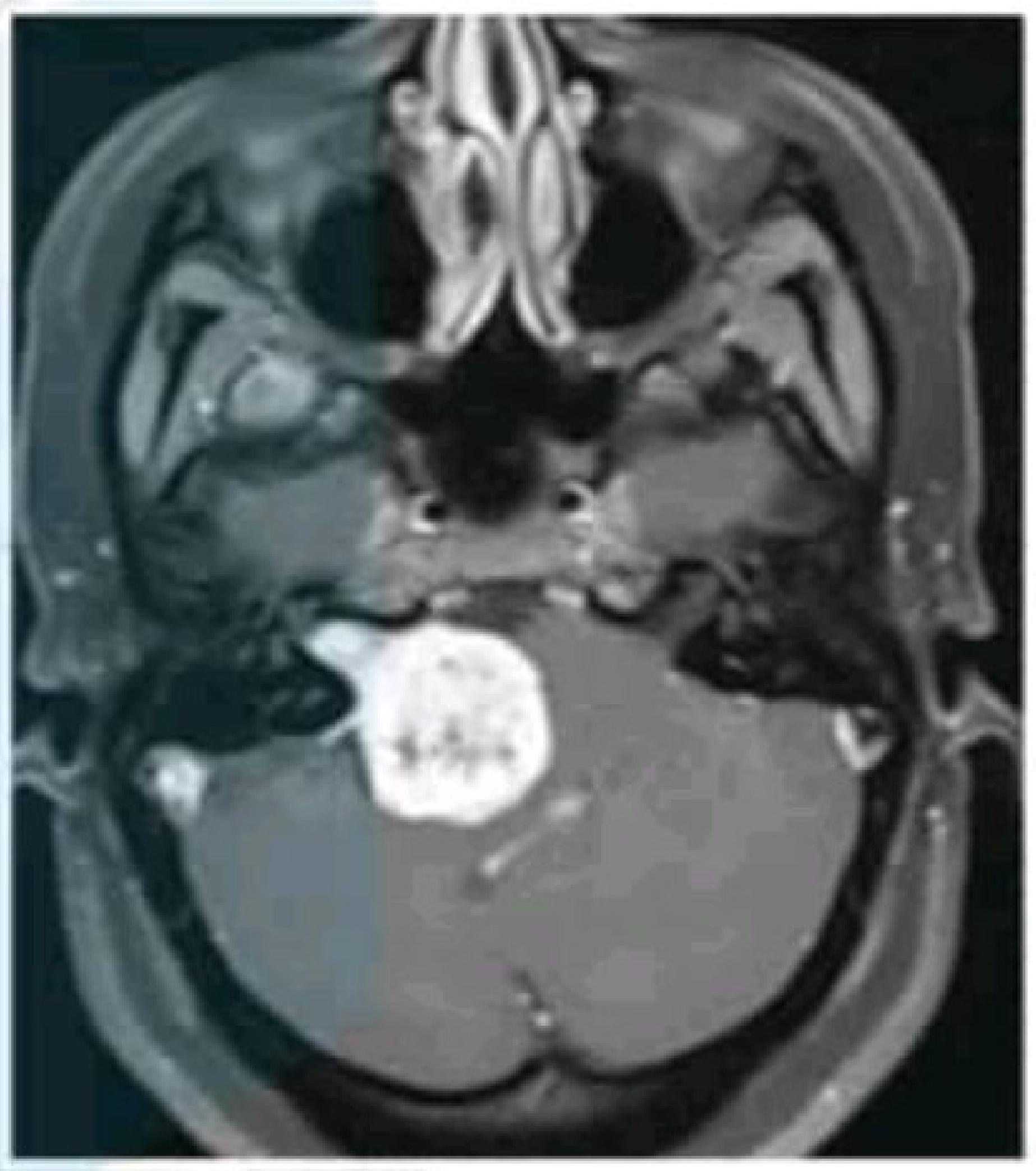


1. Meningioma

- Dural based mass
- Homogenously enhanced
- **Dural tail** is present
- Low grade tumor, F>M
- Associated with NF type 2
- Sometimes-**Volcano sign is seen**

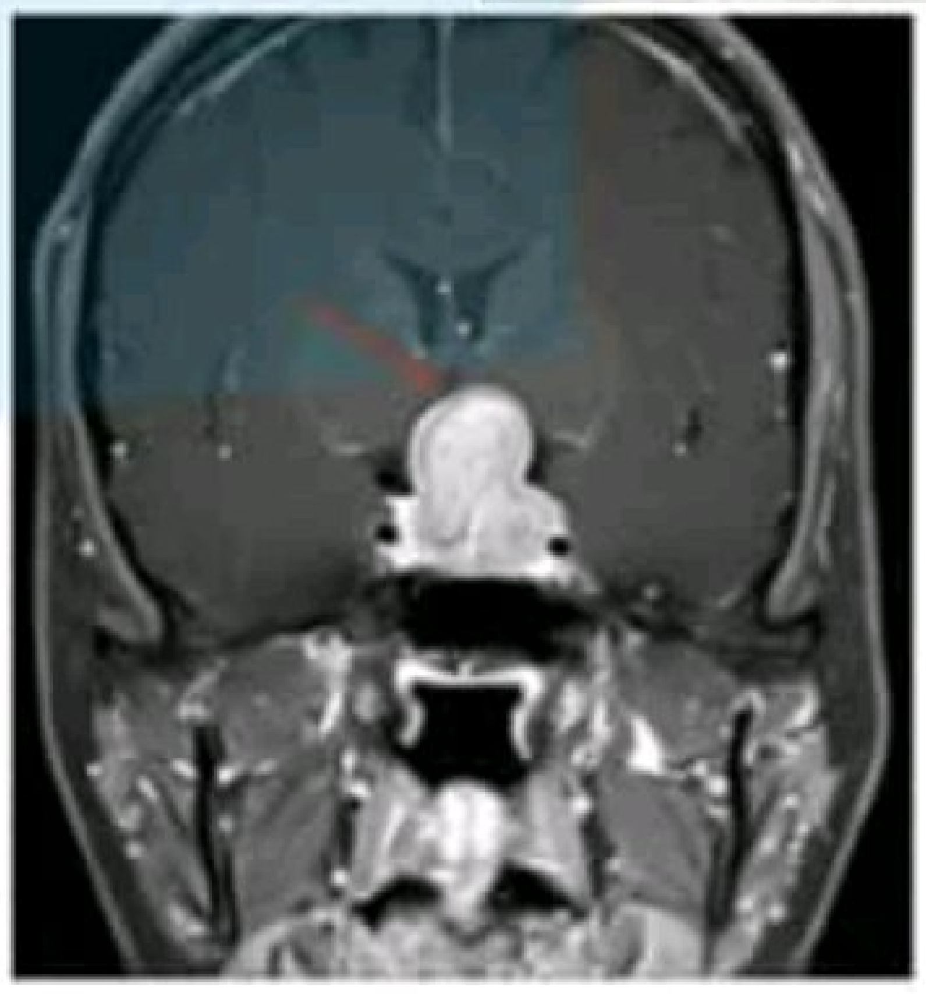


2. Vestibular Schwannoma (Acoustic Neuroma)



- CP angle tumor extending into the internal aurditory canal
- Causes sesorinueral hearing loss (SNHL)
- Role of Gamma Knife Radiotherapy in this tumor.
- Associated with Neurofibromatosis Type 2
- **ICE-CREAM CONE APPEARANCE ON MRI**

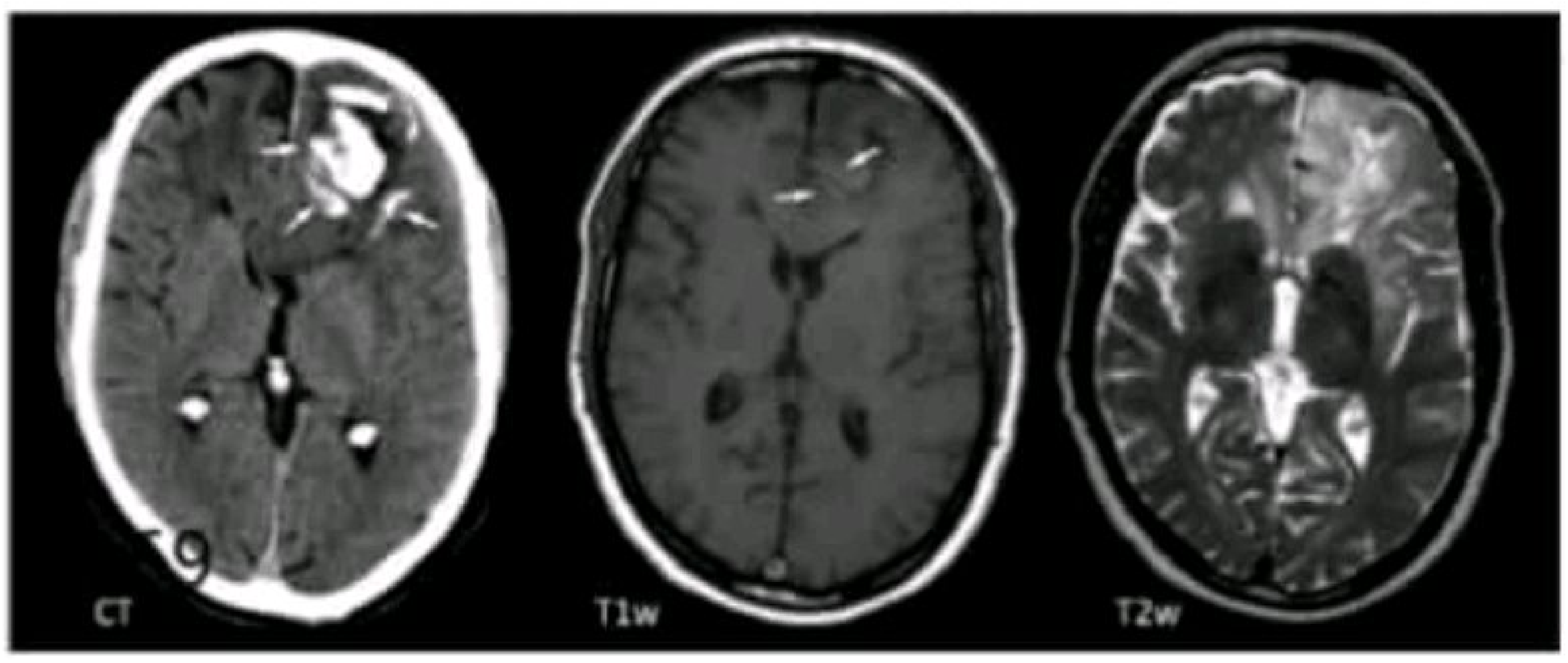
3. Pituitary Macroadenoma



- Pituitary tumor
- Indented in middle due to sella turcica.
- **SNOWMAN appr or FIGURE of 8 Appearance**
- C/F- Visual loss due to compression of the optic chiasma

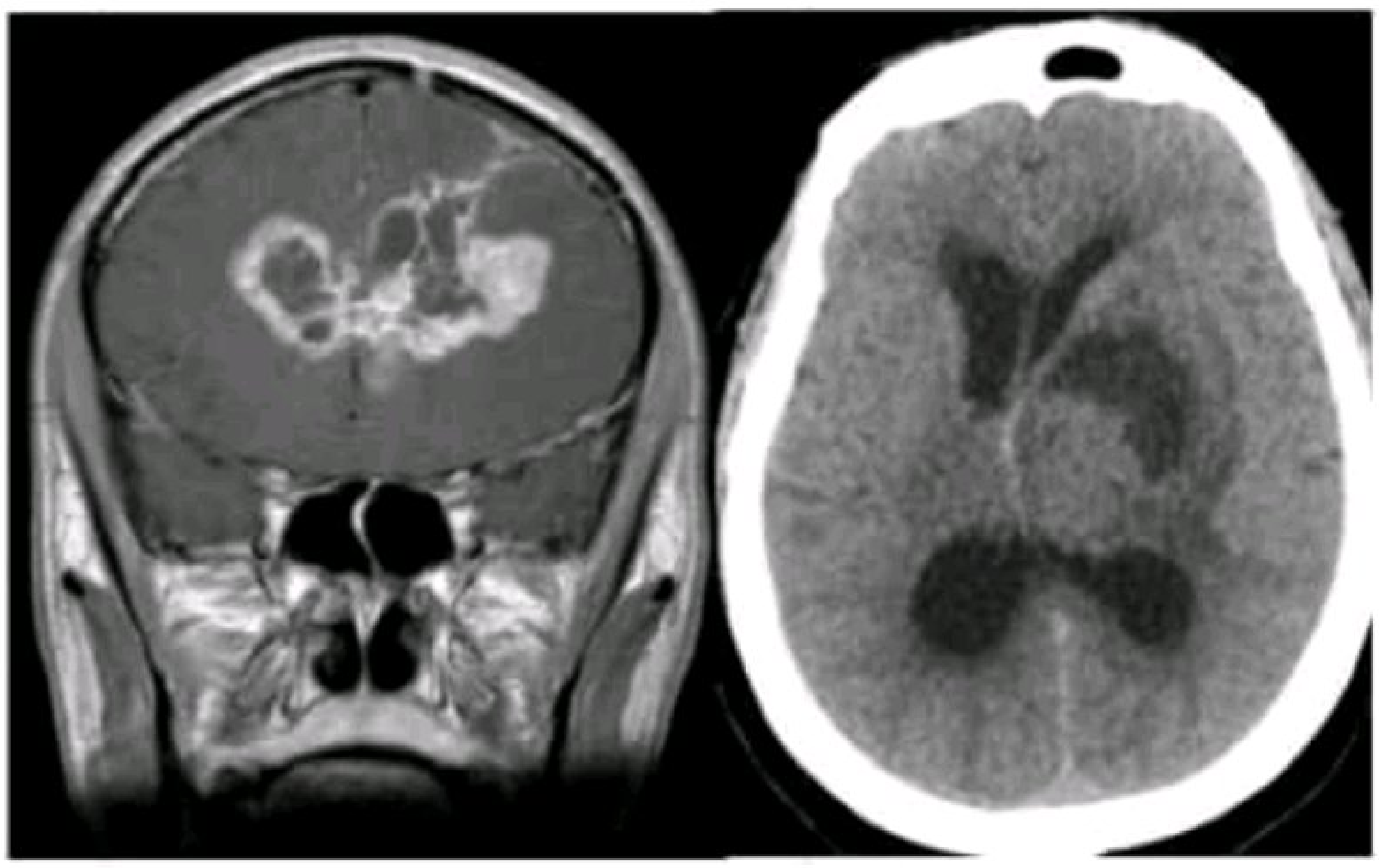
4. Oligodendroglioma

- Intraparenchymal lesion
- With areas of calcification
- Most important glial tumor that calcifies.
- Unlike meningioma, it is not attached to dura.



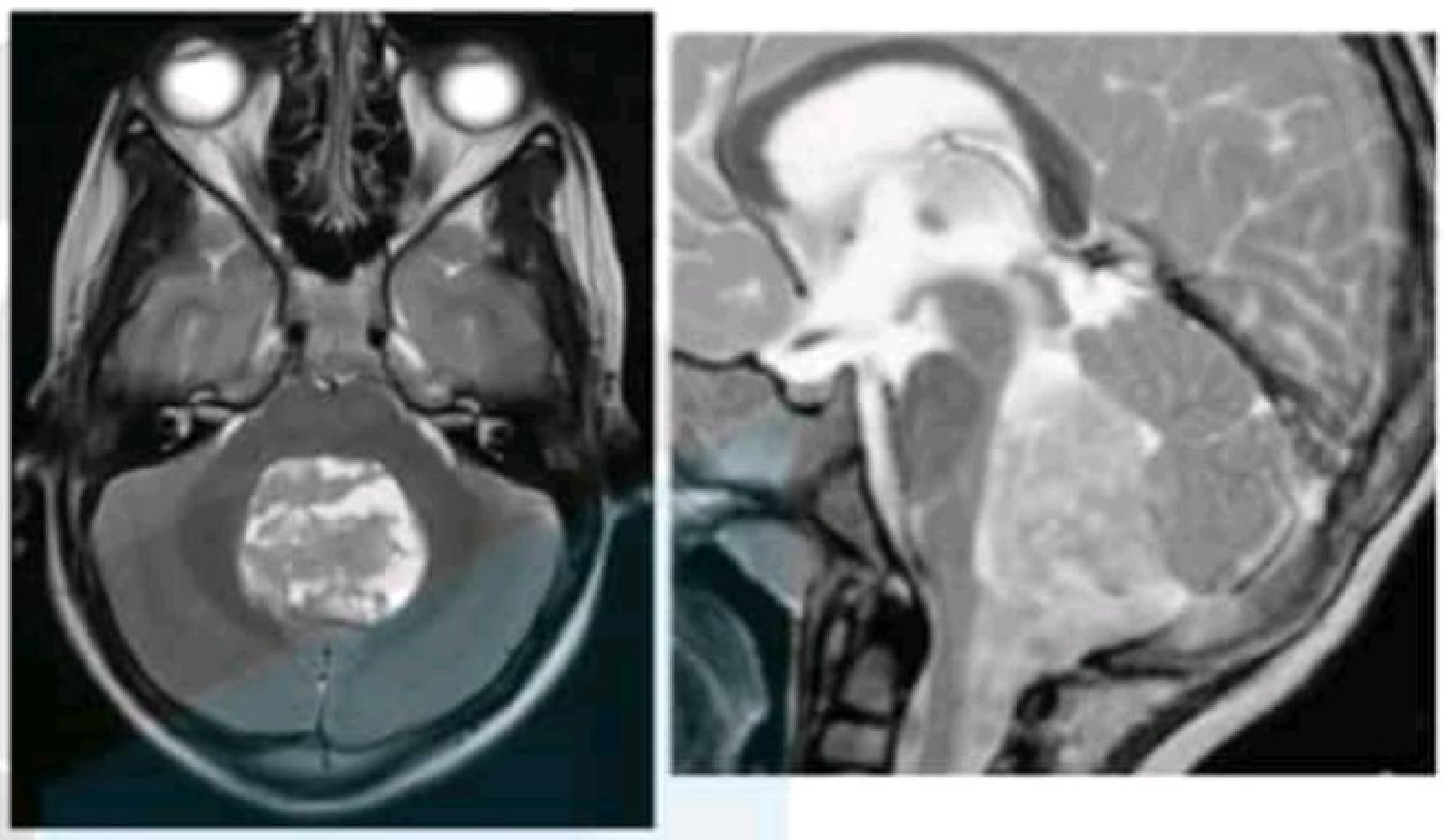
5. Glioblastoma

- Heterogenous appearance.
- Non-enhancing part on MRI is indicative of necrosis
- Disrupting the midline



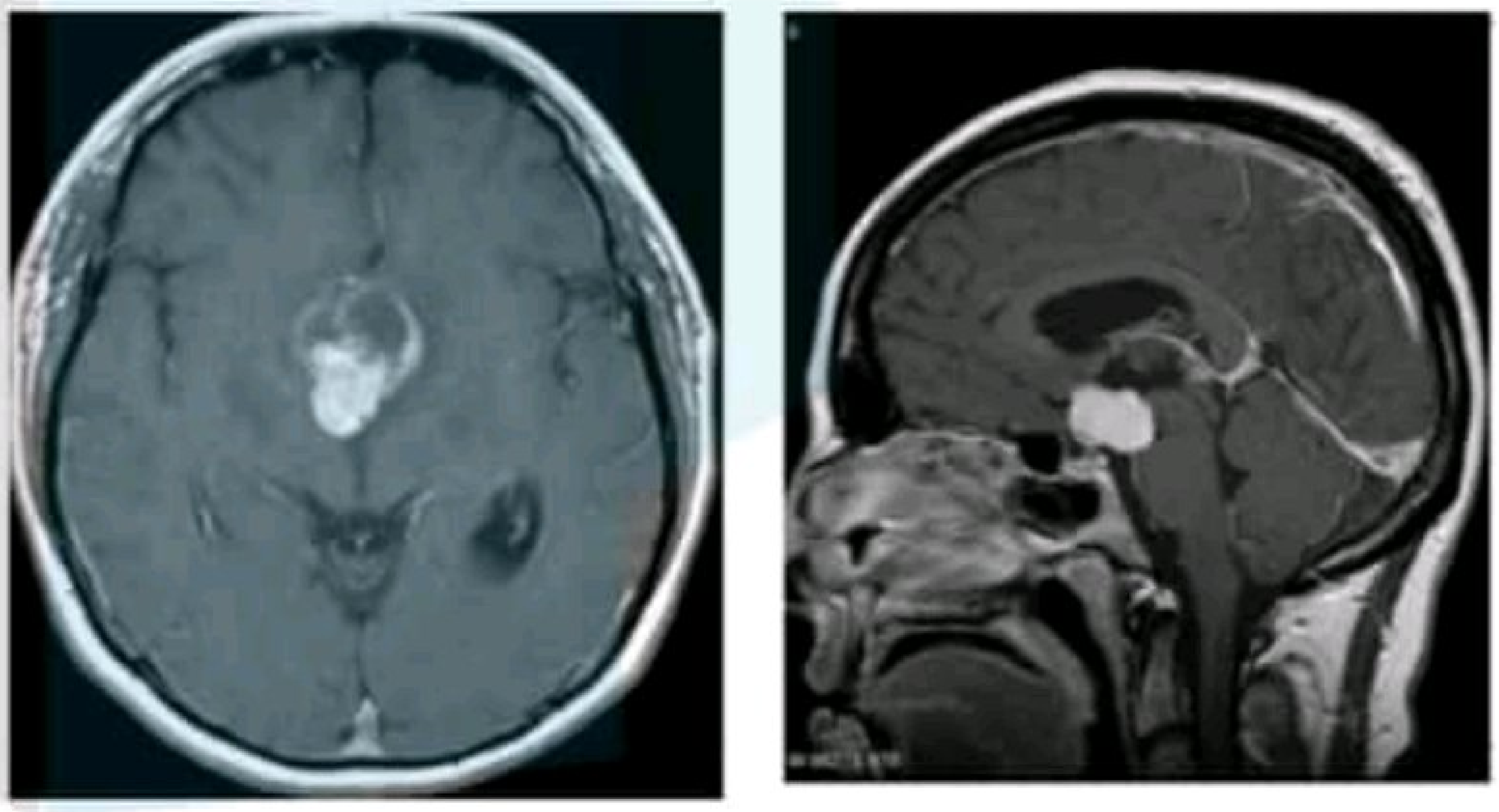
6. Ependymoma

- Tumor in the child in 4th **ventricle**
- Goes towards the midline through the Foramen of Megandie and to the CP angle through the Foramen of Luschka
- Spreads to surrounding CSF Spaces



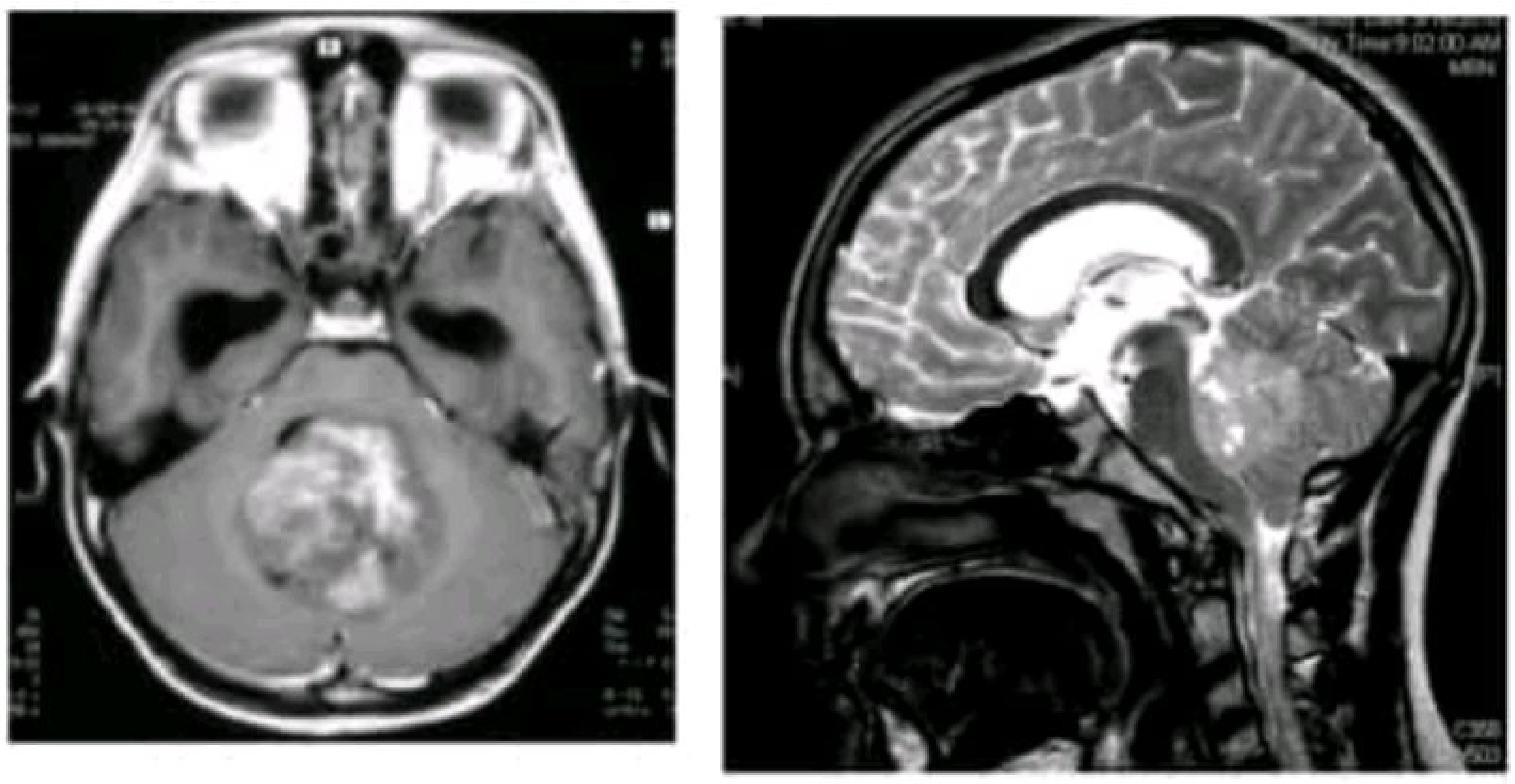
7. Craniopharyngioma

- Supresellar calcified tumor
- Rathke's pouch tumor

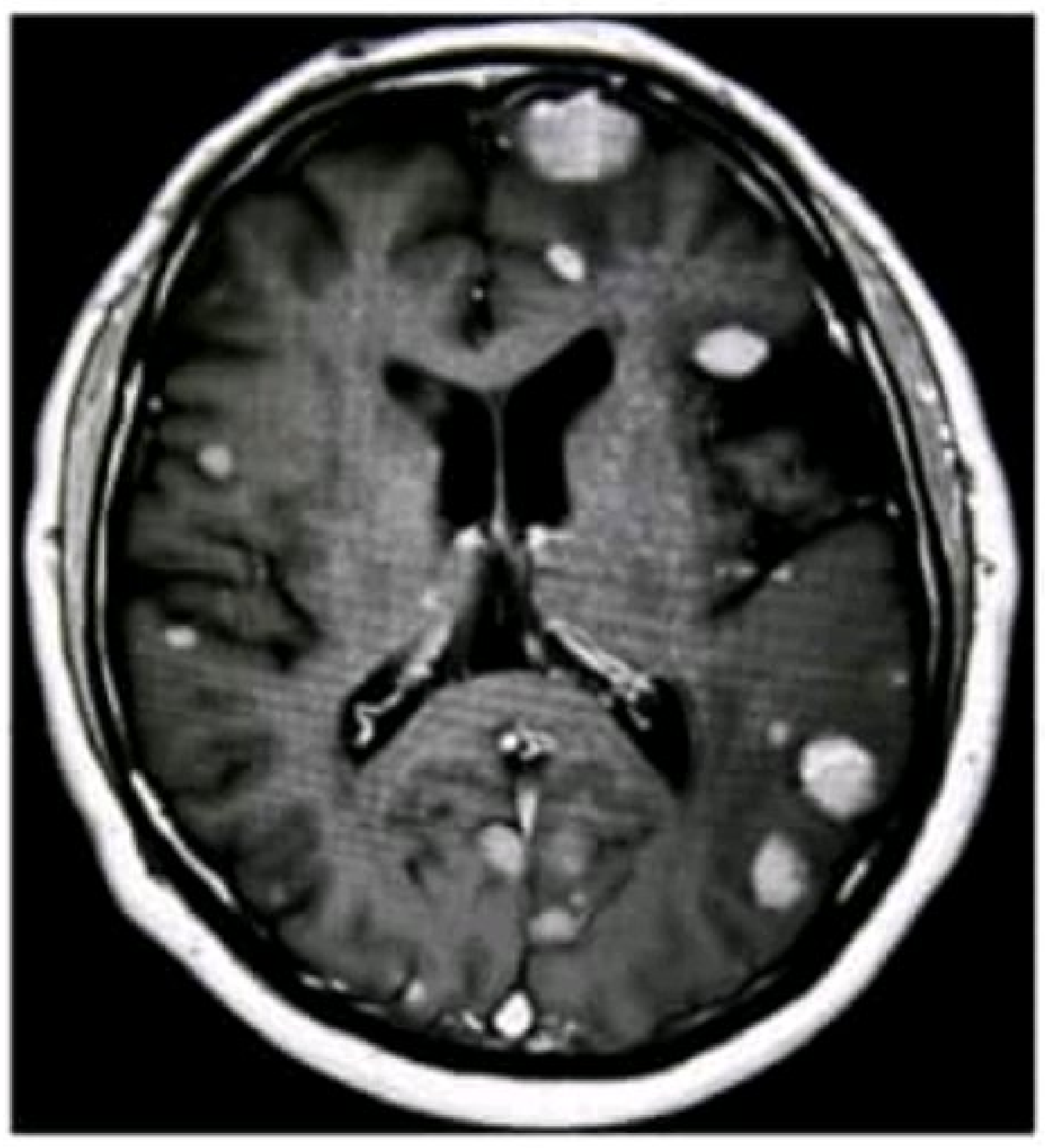


8. Medulloblastoma

- Solid tumor present in the cerebellar vermis
- Arising from the superior medullary vellum
- Seen in children
- Malignant tumor
- Spread by- CSF Drop leptomeningeal spread
- Sensitive to radiotherapy (Proton + Photon therapy)

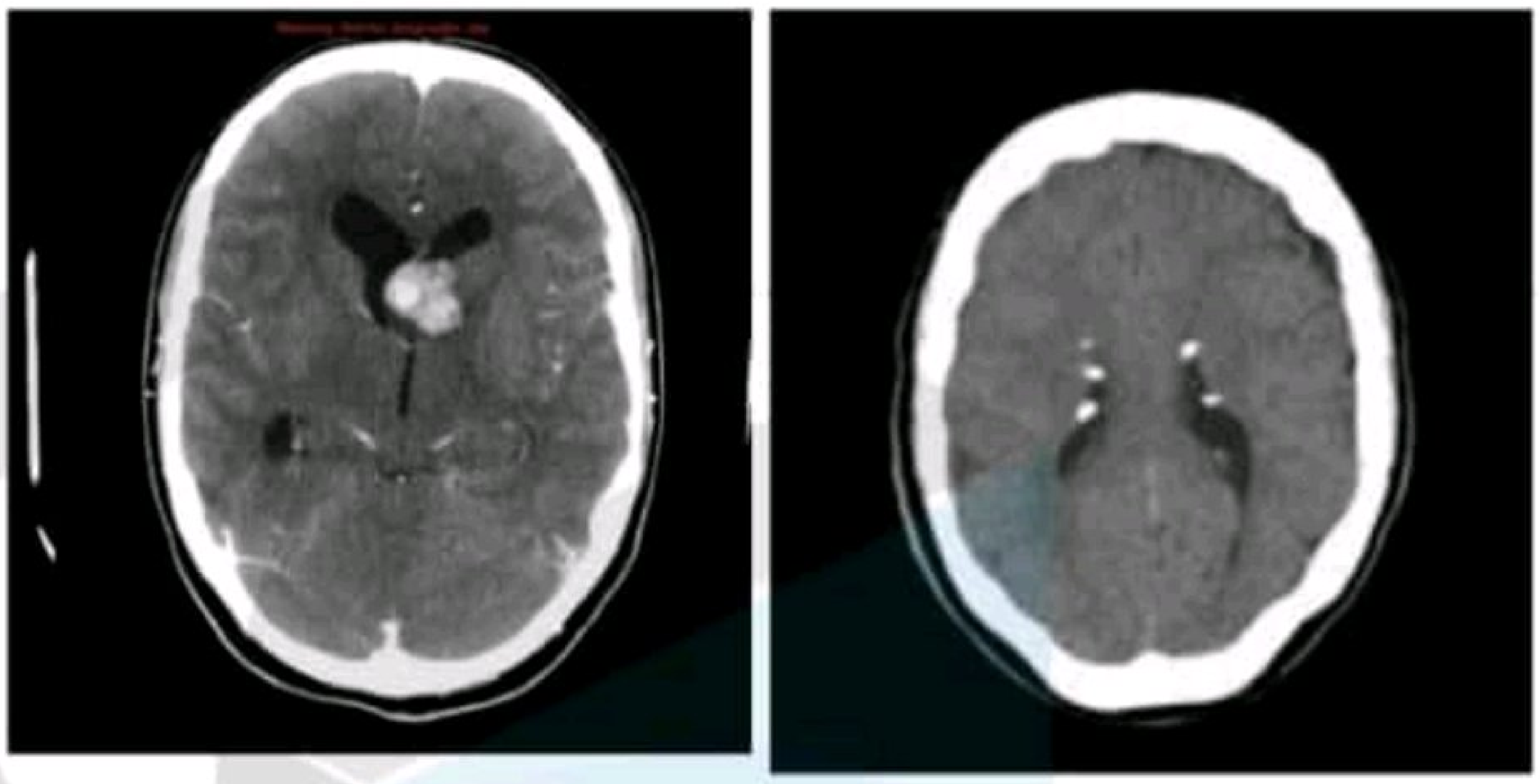


9. BRAIN METASTASIS



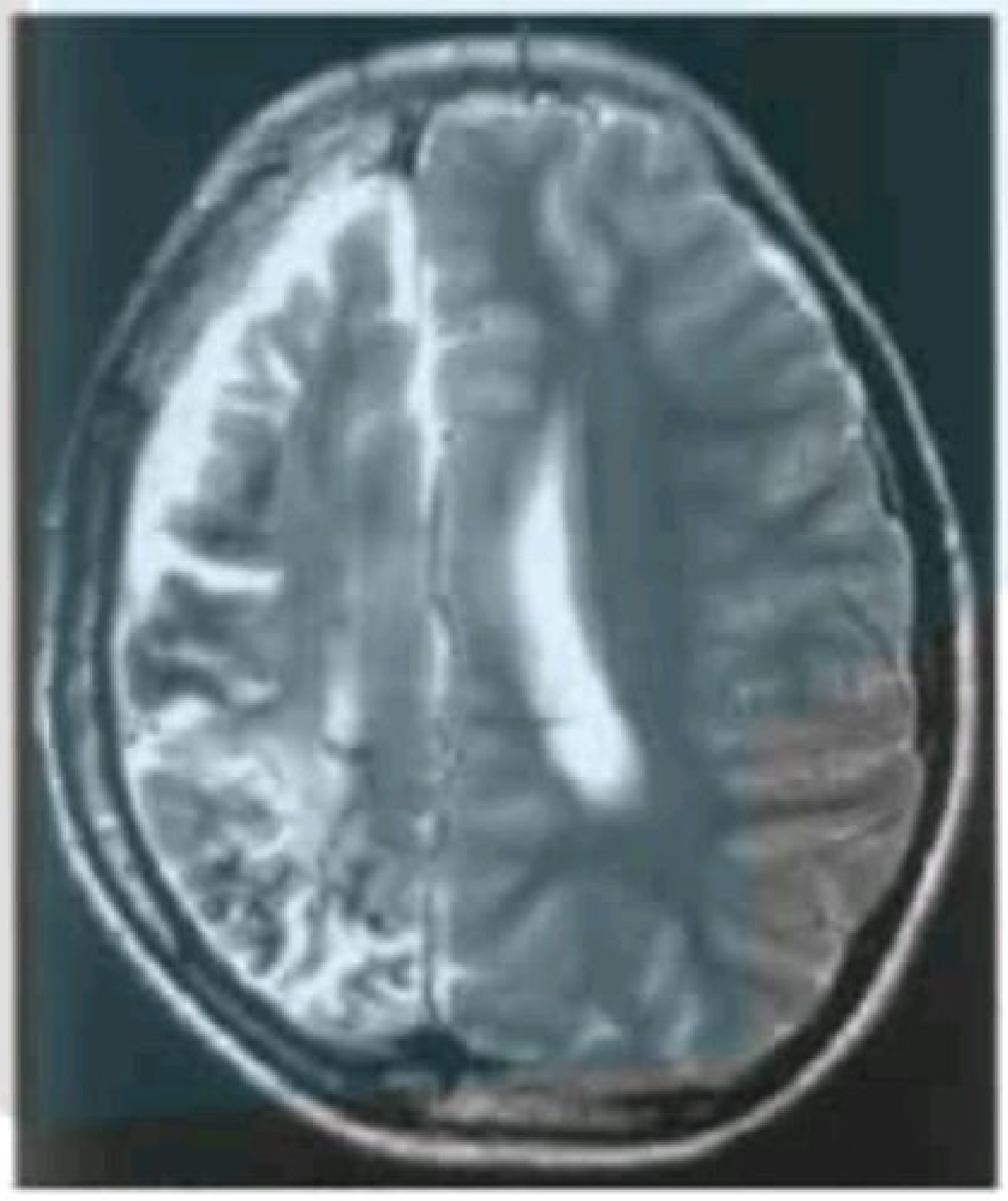
- Multifocal lesions present at the gre-white matter interface
- Involving both anterior and posterior circulation, therefore hematogenous spread from a primary
- M/C primary- Small Cell cancer of Lung

10. Tuberous Sclerosis



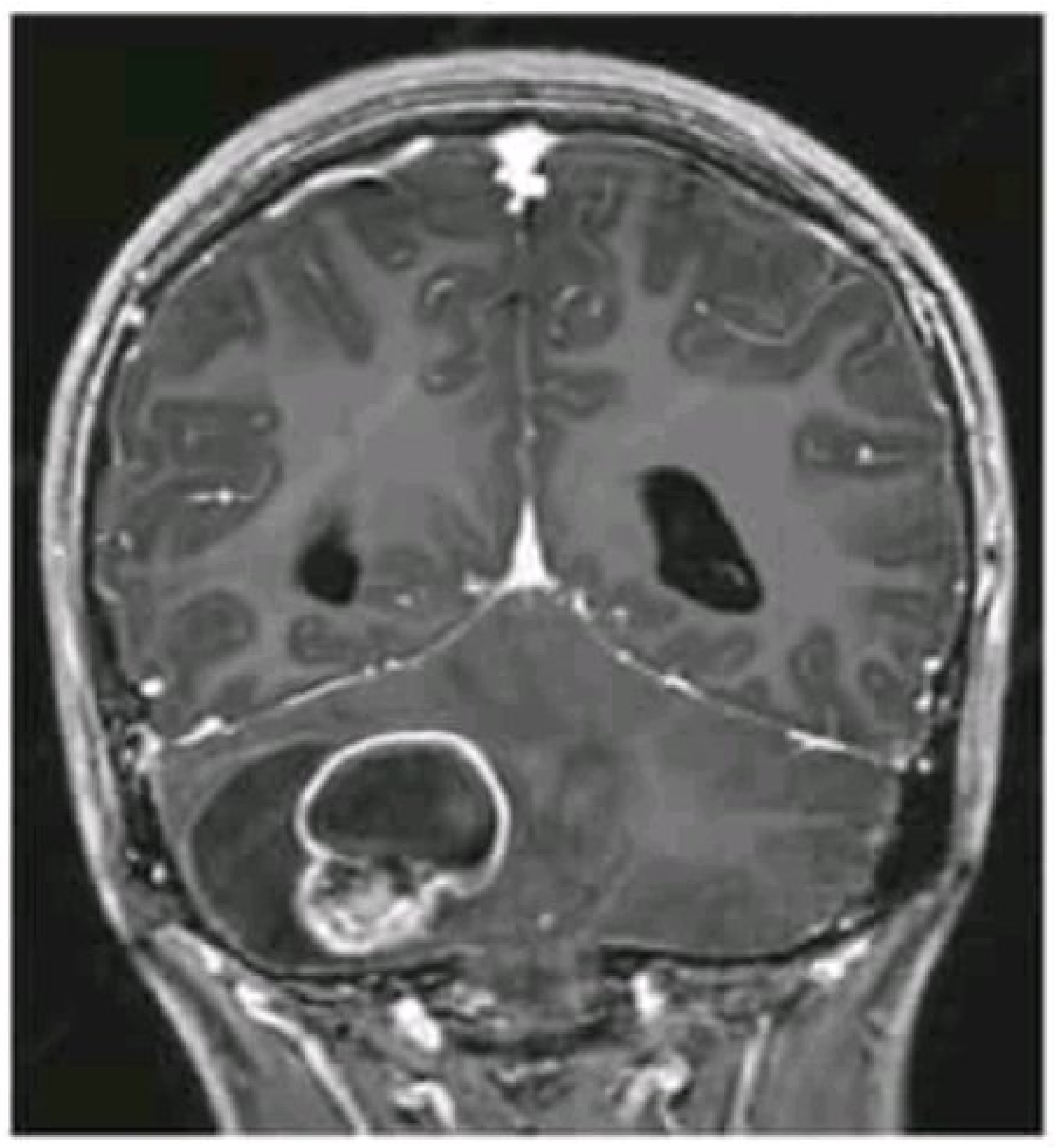
- Sub-ependymal calcific nodules on a CT Scan
- Or Sub-ependymal Giant cell Astrocytoma (SEGCA) at Foramen of Monroe

11. Sturge Weber Syndrome



- Hemiatrophy of brain along with
- Gyral Tram-track appearance due to calcification

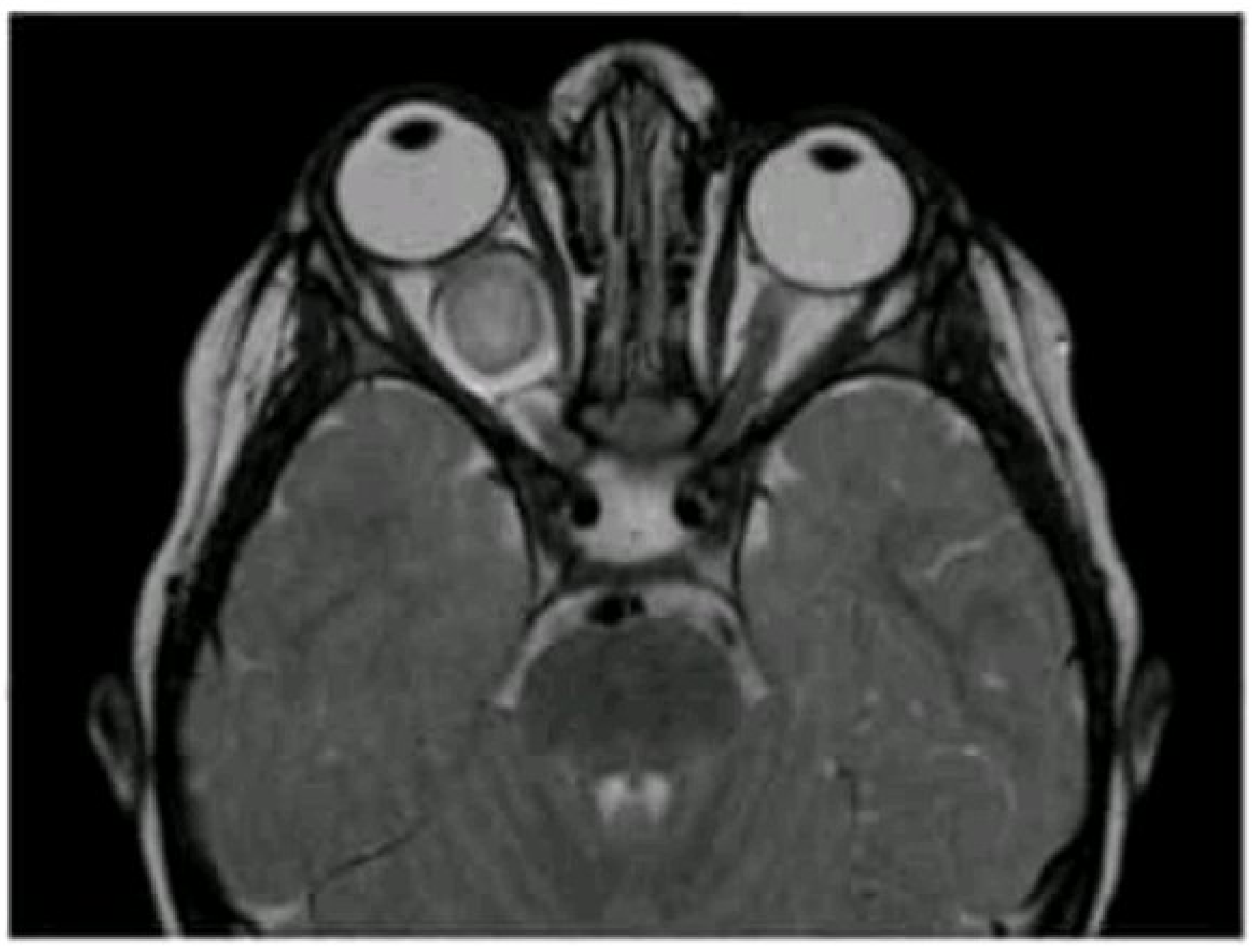
12. Hemangioblastoma Cerebellum



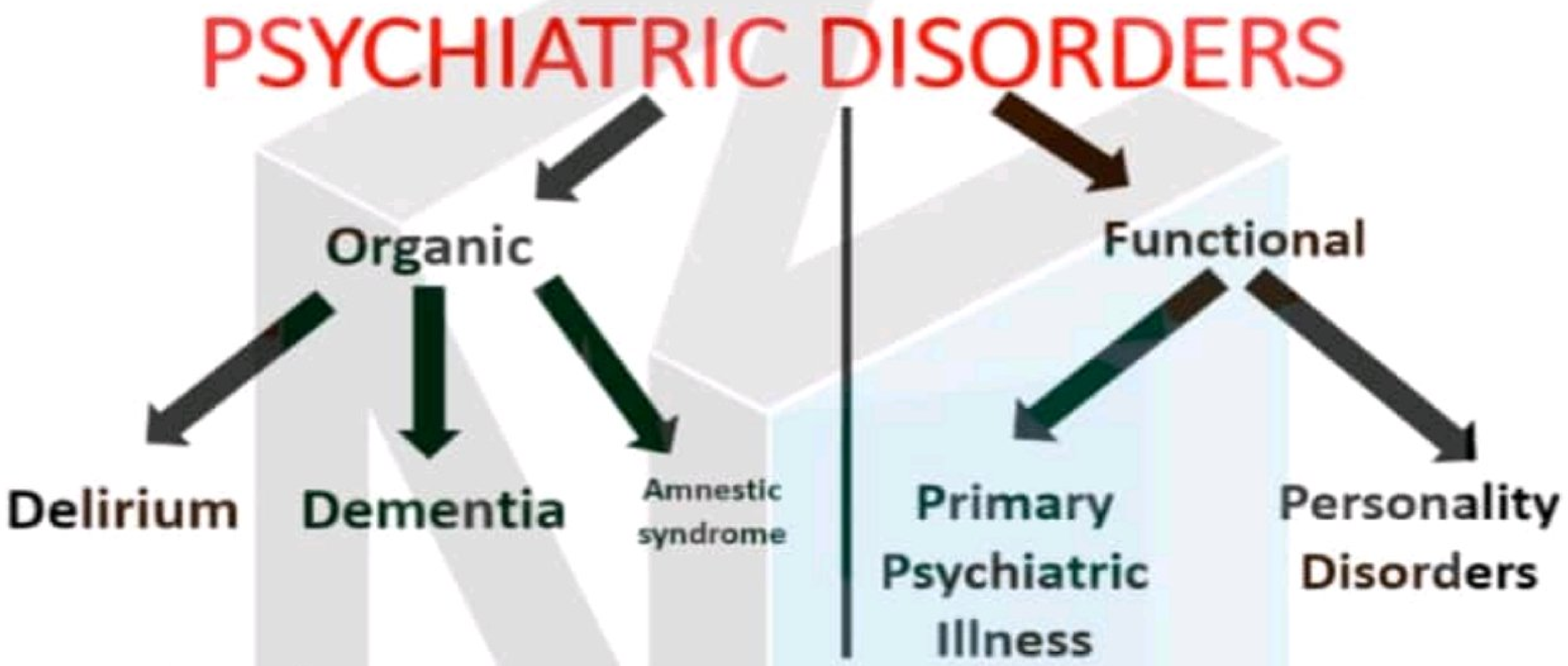
- Adult tumor
- Cystic lesion in cerebellum
- Solitary Mural Nodule
- A/w **Voh-Hippel Lindau Disease**

13. Optic Nerve Glioma/ Pilocytic Astrocytoma

- Fusiform enlargement of the optic nerve behind the globe.
- A/w Neurofibromatosis Type 1



Clinical Differential diagnosis in Psychaitry



PSYCHIATRIC DISORDERS

Organic

Delirium

Dementia

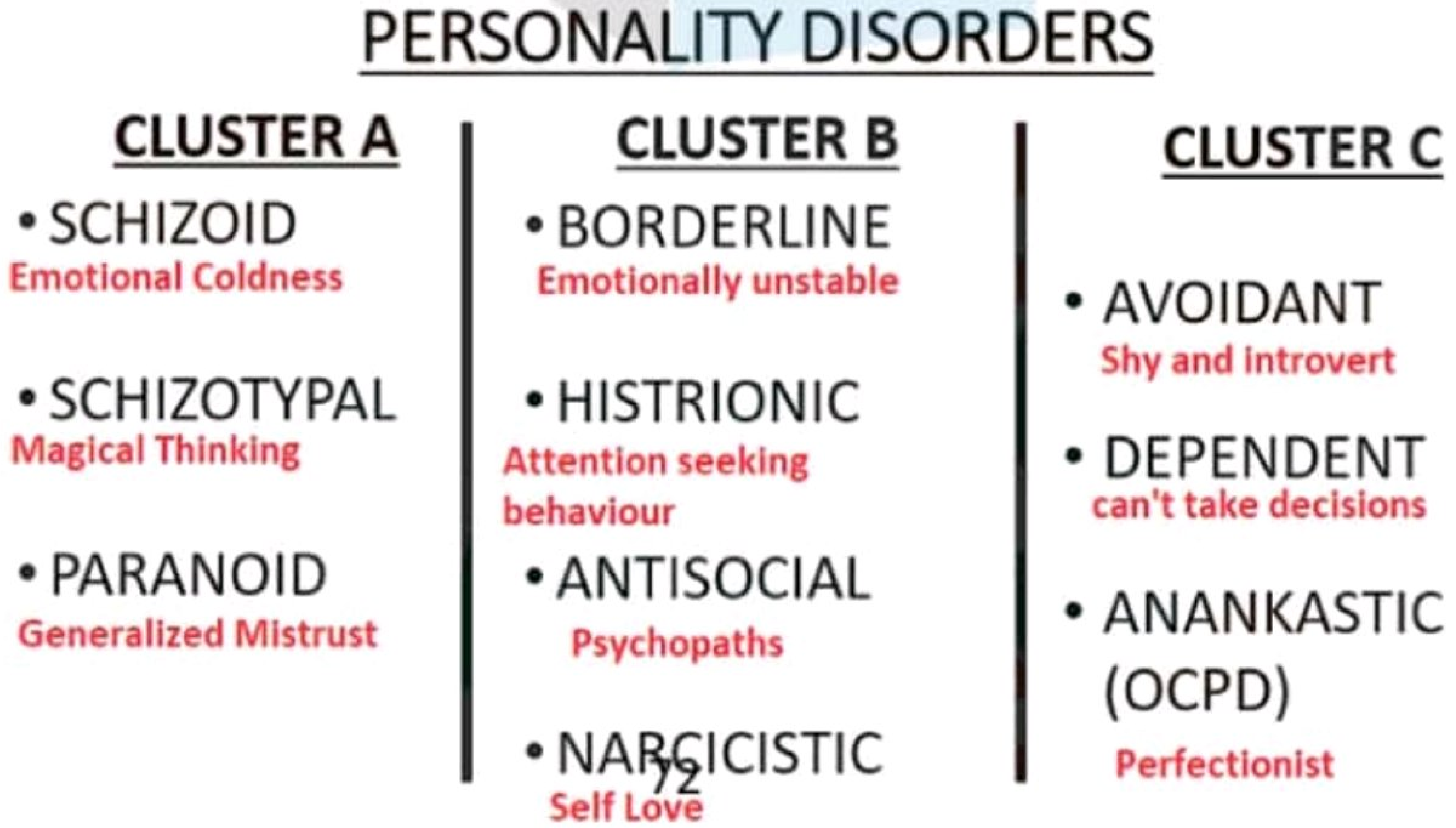
Amnestic syndrome

Functional

Primary Psychiatric Illness

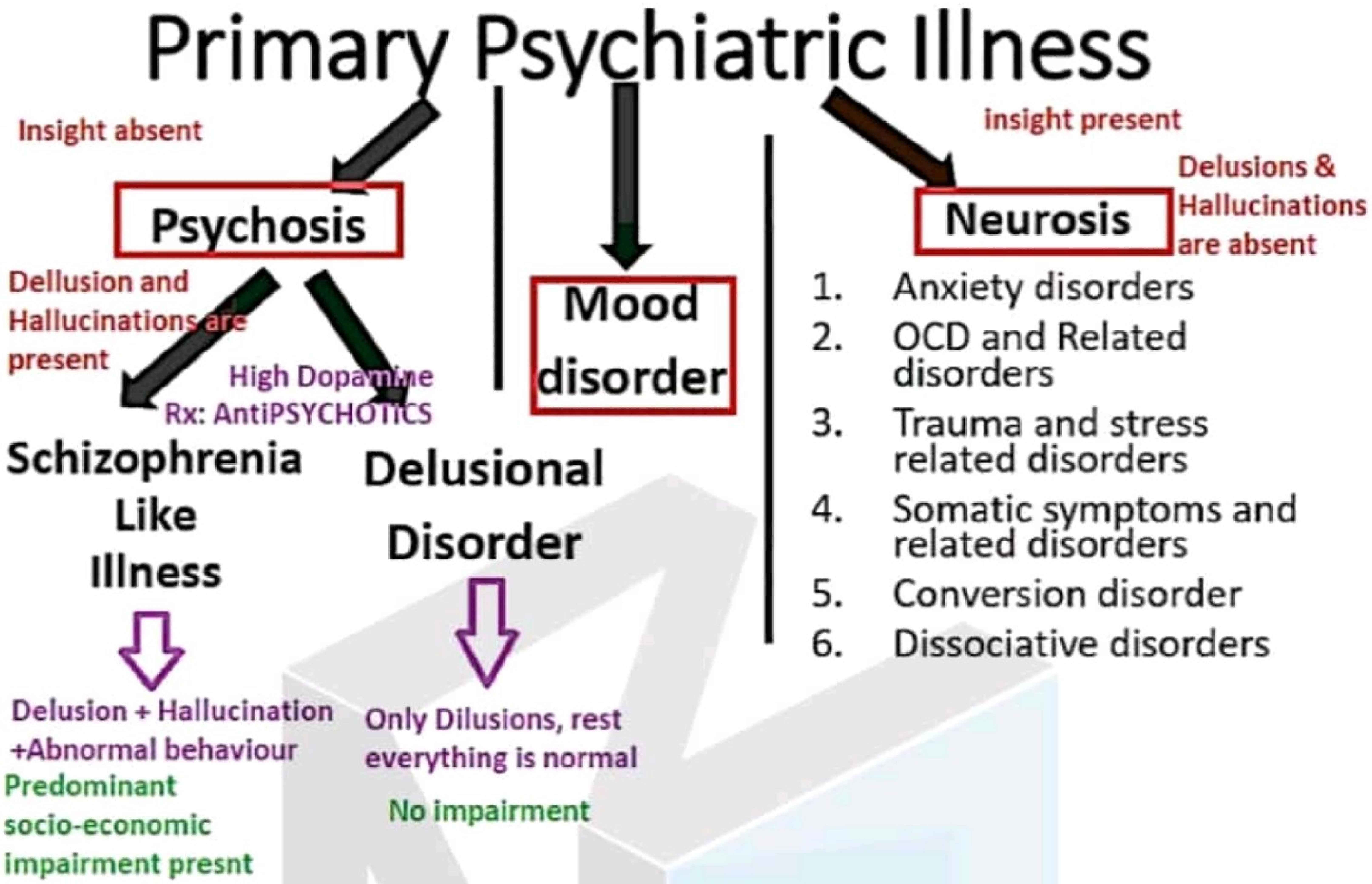
Personality Disorders

- **Delirium:** Altered sensorium
- **Dementia:** Clear Sensorium
- **Amnestic Syndrome (Wernicke Korsakoff) :** **Only amnesia + CONFABULATION (filling of gaps of recent memory)**



PERSONALITY DISORDERS

CLUSTER A	CLUSTER B	CLUSTER C
• SCHIZOID Emotional Coldness	• BORDERLINE Emotionally unstable	• AVOIDANT Shy and introvert
• SCHIZOTYPAL Magical Thinking	• HISTRIONIC Attention seeking behaviour	• DEPENDENT can't take decisions
• PARANOID Generalized Mistrust	• ANTISOCIAL Psychopaths	• ANANKASTIC (OCPD) Perfectionist
	• NARCICISTIC Self Love	



Primary Psychiatric Illness

Insight absent

Psychosis

Dellusion and Hallucinations are present

High Dopamine

Rx: AntiPSYCHOTICS

Schizophrenia Like Illness

Delusion + Hallucination +Abnormal behaviour

Predominant socio-economic impairment presnt

Delusional Disorder

Only Dilusions, rest everything is normal

No impairment

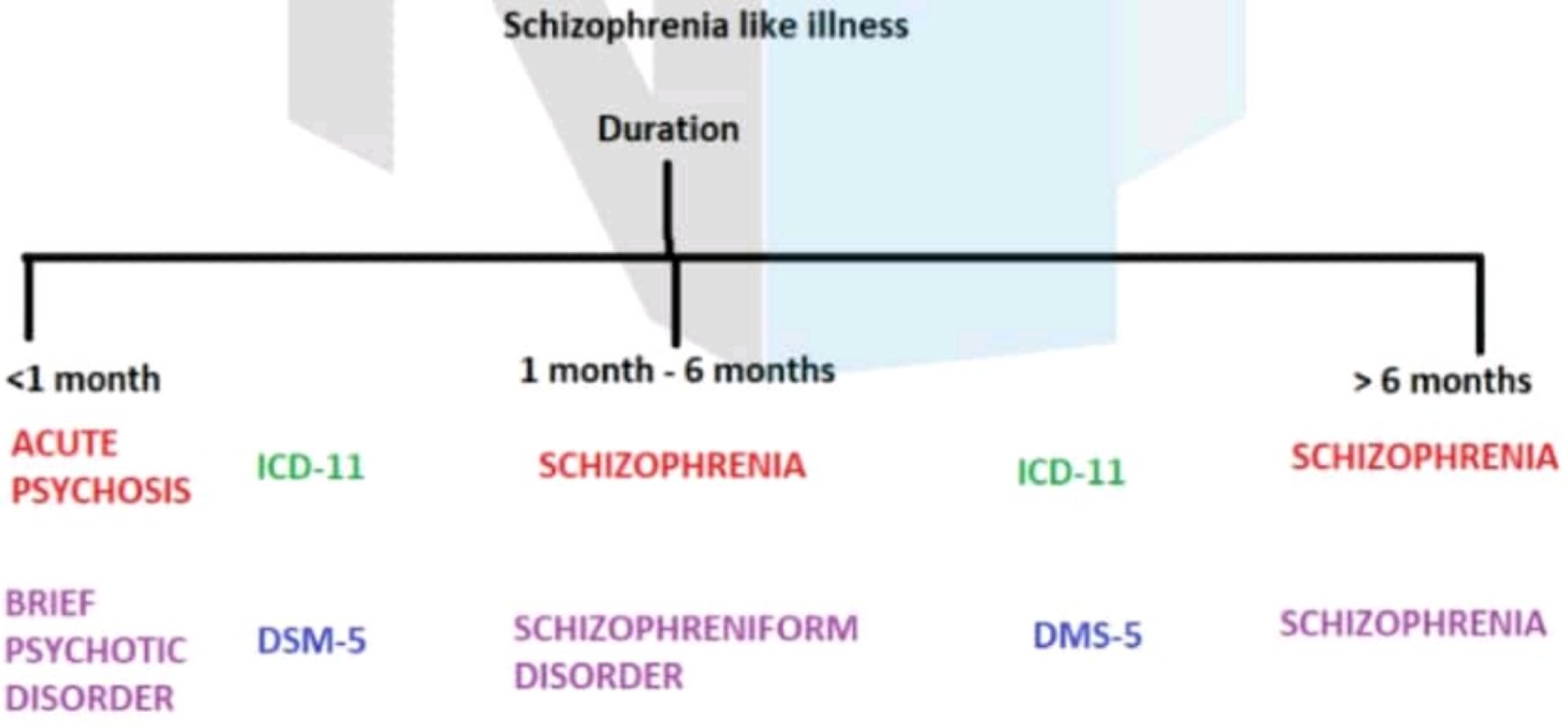
Mood disorder

insight present

Neurosis

Delusions & Hallucinations are absent

1. Anxiety disorders
2. OCD and Related disorders
3. Trauma and stress related disorders
4. Somatic symptoms and related disorders
5. Conversion disorder
6. Dissociative disorders



Schizophrenia like illness

Duration

<1 month

ACUTE PSYCHOSIS — ICD-11

BRIEF PSYCHOTIC DISORDER — DSM-5

1 month - 6 months

SCHIZOPHRENIA — ICD-11

SCHIZOPHRENIFORM DISORDER — DMS-5

> 6 months

SCHIZOPHRENIA

SCHIZOPHRENIA

FOR ALL PSYCHOTIC DISORDERS- DOC IS ANTIPSYCHOTICS

ANTI-PSYCHOTICS

USES

ANTI-EMETICS
PSYCHOSIS
CHOREA
TIC DISORDER

CLASSIFICATION

TYPICAL ANTIPSYCHOTICS (NEUROLEPTICS) 1ST GENERATION	**ATYPICAL ANTIPSYCHOTICS 2ND GENERATION**
• BLOCK DOPAMINE (D2) MORE	• BLOCK 5-HT2 (SEROTONIN) MORE
• CONTROL POSITIVE SYMPTOMS	• CONTROL POSITIVE + NEGATIVE SYMPTOMS
• S/E: MORE RISK OF EXTRAPYRAMIDAL SYMPTOMS, PROLACTIN INCREASE	• S/E: MORE RISK OF OBESITY, DIABETES, METABOLIC SYNDROME

TYPICAL ANTIPSYCHOTICS

CHEMICAL CLASSIFICATION

PHENOTHIAZINE	-AZINE	CHLORPROMAZINE THIORIDAZINE FLUPHENAZINE PERPHENAZINE
THIOXANTHENES	-THIX-	THIOTHIXENE FLUPENTHIXOL ZUCLOPENTHIXOL
BUTYROPHENONE	-RIDOL	HALOPERIDOL DROPERIDOL BENPERIDOL PENFLURIDOL
MISCELLANEOUS	-	LOXAPINE MOLINDONE PIMOZIDE

POTENCY SEQUENCE:
Butyrophenone> Thioxanthene> Phenothiazine

Side effects sequence:
Butyrophenone> Thioxanthene> Phenothiazine

Therefore Haloperidol is most effective but most notorious also for it side effects

ATYPICAL ANTIPSYCHOTICS

FUNCTIONAL CLASSIFICATION

RECEPTORS	HOW TO IDENTIFY		DRUGS
5-HT2 ANTAGONIST > D2 ANTAGONIST	-PINE -DONE	CLOZAPINE. OLANZAPINE. ZOTEPINE. ASENAPINE. QUETIAPINE.	ZIPRASIDONE RISPERISONE ILAPERIDONE SERTINDOLE PALIPERDONE
D1/2 PARTIAL AGONIST	-PIPRAZOLE	ARIPIPRAZOLE BREXIPIPRAZOLE	
D2 + D3 ANTAGONIST	-SULPIRIDE	SULPIRIDE LEVOSULPIRIDE AMISULPIRIDE	
5-HT1A INVERSE AGONIST	-SERIN	PIMAVANSERIN	

Pimavanserin is used for psychosis in Parkinson's Ds.

INTRAMUSCULAR DEPOT (Z TECHNIQUE)

HIGH	**HALOPERIDOL**
FIVE	**FLUPHENAZINE**
ZERO	**ZUCLOPENTHIXOL**
PRICE	**PERPHENAZINE**
P	**PALIPERDONE**
A	**ARIPIPRAZOLE**
R	**RISPERIDONE**
O	**OLANZAPINE**

SUBLINGUAL	INTRANASAL
ASENAPINE	LOXAPINE

EXTRAPYRAMIDAL SYMPTOMS

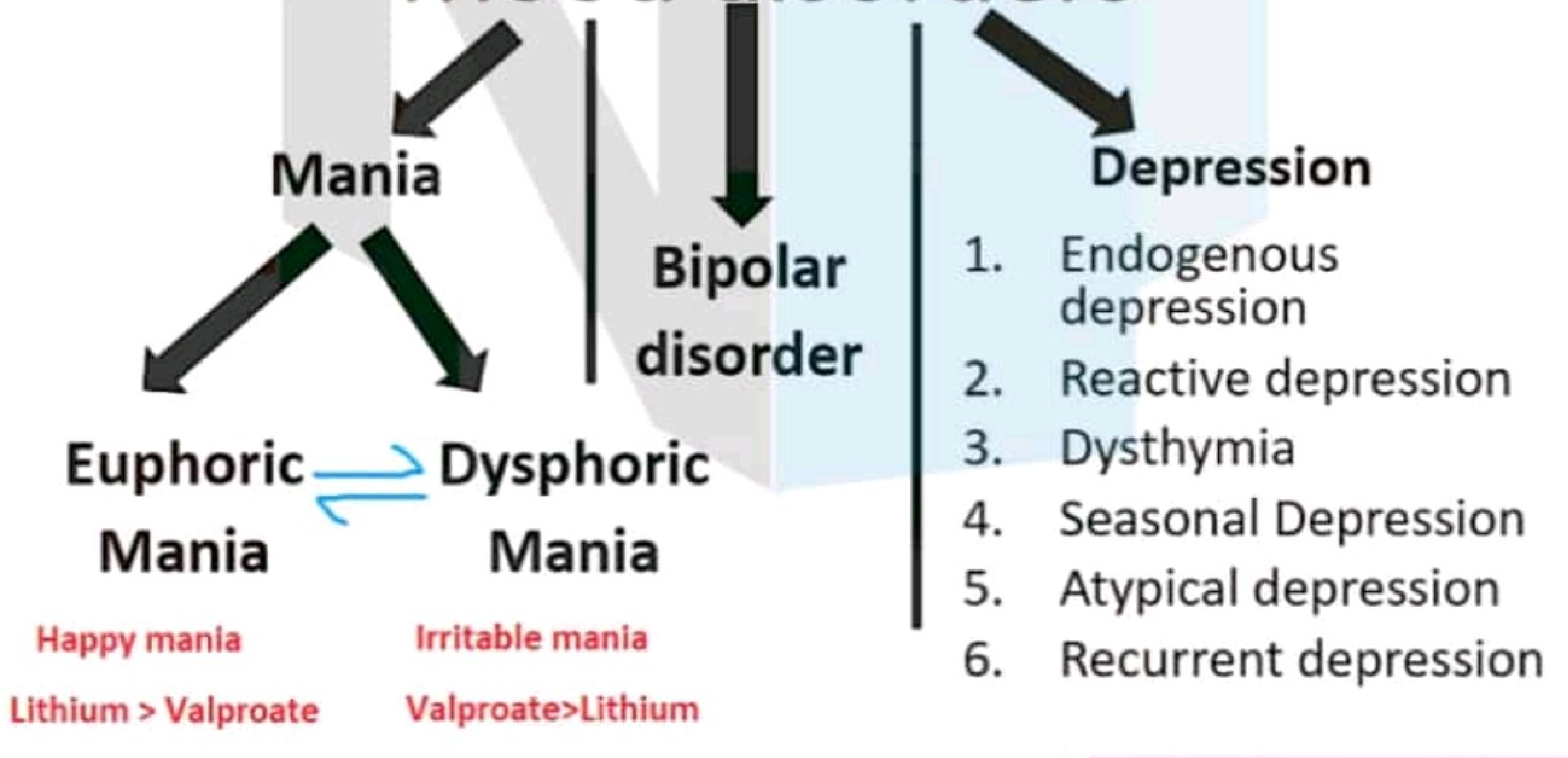
Never - APART	ONSET	FEATURES	PHARMACOTHERAPY
NEUROLEPT MALIGNANT SYNDROME	EMERGENCY	Extreme rigidity, hyperthermia, unstable blood pressure, rhabdomyolysis, myoglobinuria; can be fatal	• Dantrolene • Bromocriptine
ACUTE DYSTONIA	1-5 DAYS (FIRST)	Spasm of muscles of tongue, face, neck, back	Antiparkinsonian agent (injection) • Promethazine • Benztropine
PARKINSONISM	5-30 DAYS	Bradykinesia, rigidity, variable tremor, mask facies, shuffling gait	Antiparkinsonian agent (oral) • Benzhexol • Promethazine
AKATHISIA	5-60 DAYS Most common EPS	Subjective and objective restlessness; *not* anxiety or "agitation" Aggravated by smoking.	Propranolol > diazepam/clonazepam
RABBIT SYNDROME	MONTHS/YEARS	Perioral Tremors	Antiparkinsonian agent • Benzhexol
TARDIVE DYSKINESIA	MONTHS/YEARS (LAST)	Orofacial dyskinesia; widespread choreoathetosis	Stop drug and star Clozapine VMAT2 inhibitors • Valbenazine • Deutetrabenazine

- CLOZAPINE: Most Effective Drug, Anti-suicidal, DOC Is Resistant Psychosis

NON-SERIOUS	SERIOUS
METABOLIC SYNDROME	SEIZURES
OBESITY	AGRANULOCYTOSIS (DOSE INDEPENDENT)
TYPE 2 DIABETES	MYOCARDITIS
HYPERSALIVATION	
SEDATION	

- Thioridazine: Retinal Degeneration
- Weight Gain and Metabolic syndrome (Maximum): Olanzapine > Clozapine
- Risperidone: Prolactin Increase (maximum among Atypical antipsychotics)
- QT prolongation: Ziprasidone, Sertindole, Quetiapine
- Cataract: Quetiapine > Clozapine

Mood disorders



Mania

Euphoric Mania ⇄ **Dysphoric Mania**

Happy mania — Irritable mania

Lithium > Valproate — Valproate>Lithium

Bipolar disorder

Depression

1. Endogenous depression
2. Reactive depression
3. Dysthymia
4. Seasonal Depression
5. Atypical depression
6. Recurrent depression

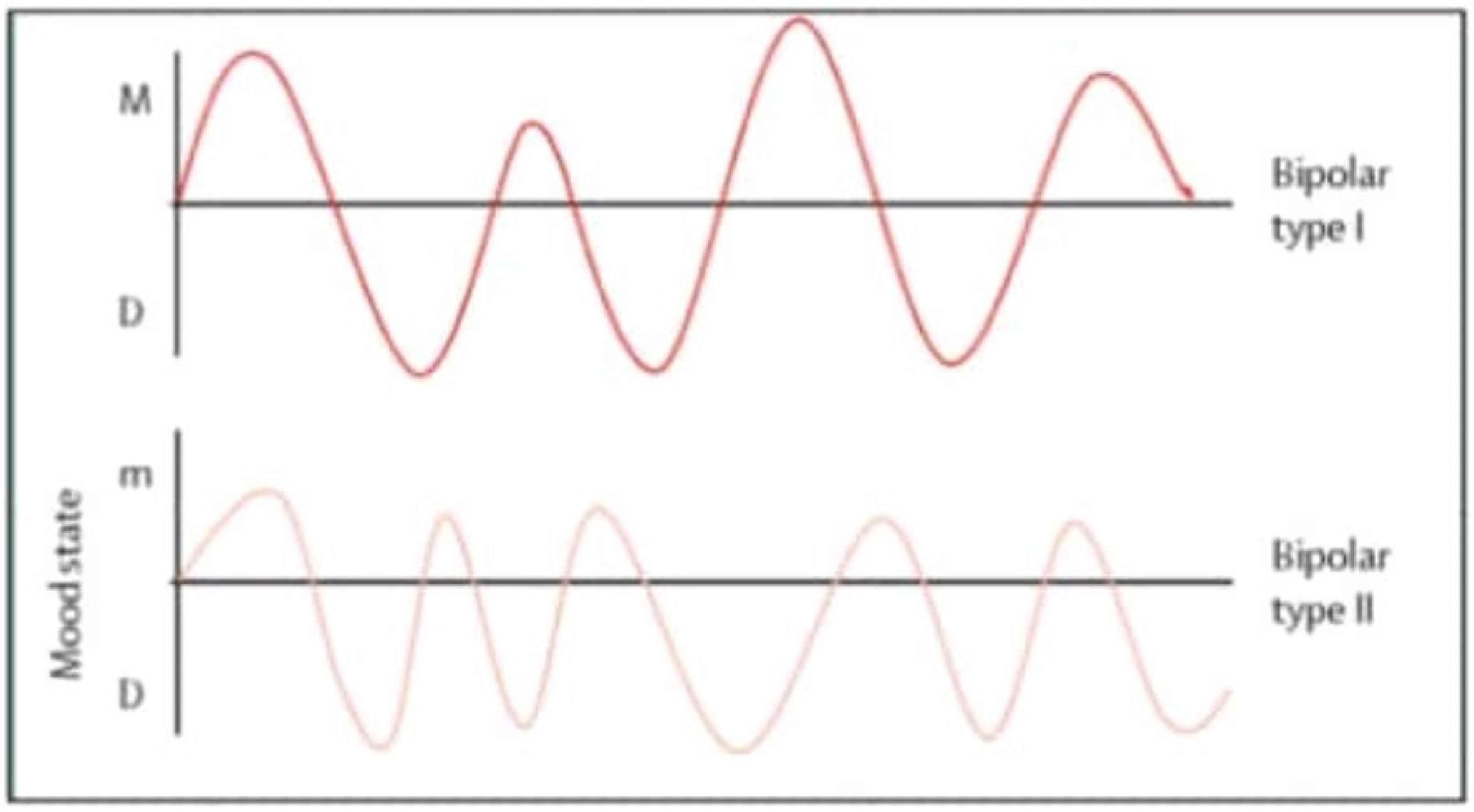
Mania:
1. 7 days reqd for diagnosis
2. Delusion of grandiosity (psychotic symptom) may be present or absent
3. May need hospitalization

Hypomania:
1. 4 days reqd for diagnosis
2. Delusion of grandiosity is always absent
3. Always mentioned on an OPD basis

Common features of mania:
1. Decreased need for sleep
2. Talkativeness
3. Energetic

Neurotransmitters:
Increase in DA and NE

Bipolar disorders



1. Bipolar affective disorder type 1 (BPAD-1): **Mania + Depression**

2. Bipolar affective disorder type 2 (BPAD-2): **Hypomania + Depression**

Rx: Mood Stabilizers- Lithium and Valproate

Depression- Major Depressive Disorder (MDD)

- Minimum Duration required for diagnosis = 2 weeks
- If depressed mood lasts for >2 yrs → DYSTHYMIA **(Neurotic Depression)**

Types:

1. Depression with psychosis (Severe Depression)

- Has delusions of guilt, sin, nihilism
- Suicide provoking hallucinations
- Rx: SSRI + Antipsychotics (D2 Blocker)

2. Depression without psychosis

- No delusions
- Rx: SSRI

- **Endogenous Depression → Melancholia**
  - **Without a stress factor**
- **Reactive Depression – with a stress factor**
- **Dysthymia- Depression for >2yrs**
- **Seasonal Depression**
  - **Depression happening only in WINTERS**
  - **Time required: 2 years**
  - **Rx: Light therapy/ Phototherapy**
- **Atypical Depression:**
  - **Reversal of symptoms- Increased sleep and appetite**
- **Recurrent Depression**
  - **Two distinct episodes of depression 2 months apart, where the patient is normal within these 2 months**

MOOD STABILIZERS

Low	LITHIUM
V	VALPROATE
O	OXCARBAZEPINE, CARBAMAZEPIINE
L	LAMOTRIGINE
T	TOPIRAMATE
A	ANTIPSYCHOTICS
Ge	GABAPENTINE

Anti-epileptics with mood stabilizing effects

*OXCARBAZEPINE and TOPIRAMATE are not approved yet.

LITHIUM

USES
BIPOLAR DISORDER
HYPNIC HEADACHE
ANTISUICIDAL DRUG (ALSO CLOZAPINE)
RESISTANT DEPRESSION

Contraindication: During Breast-Feeding

PHARMACOKINETICS	
ROUTE	ORAL, IV
HALF LIFE	24 HOURS
MONITORING	12 HOURS AFTER LAST DOSE
METABOLISM	NO
EXCRETION	URINE > SWEAT, SALIVA, MILK

• SERUM LEVEL OF LITHIUM

0.6 – 1.0 meq/L	Maintenance of bipolar disorder
1.0 – 1.5 meq/L	Acute mania
> 1.5 meq/L	Toxicity
> 2.0 meq/L	Hospitalization
> 3–4 meq/L	Hemodialysis

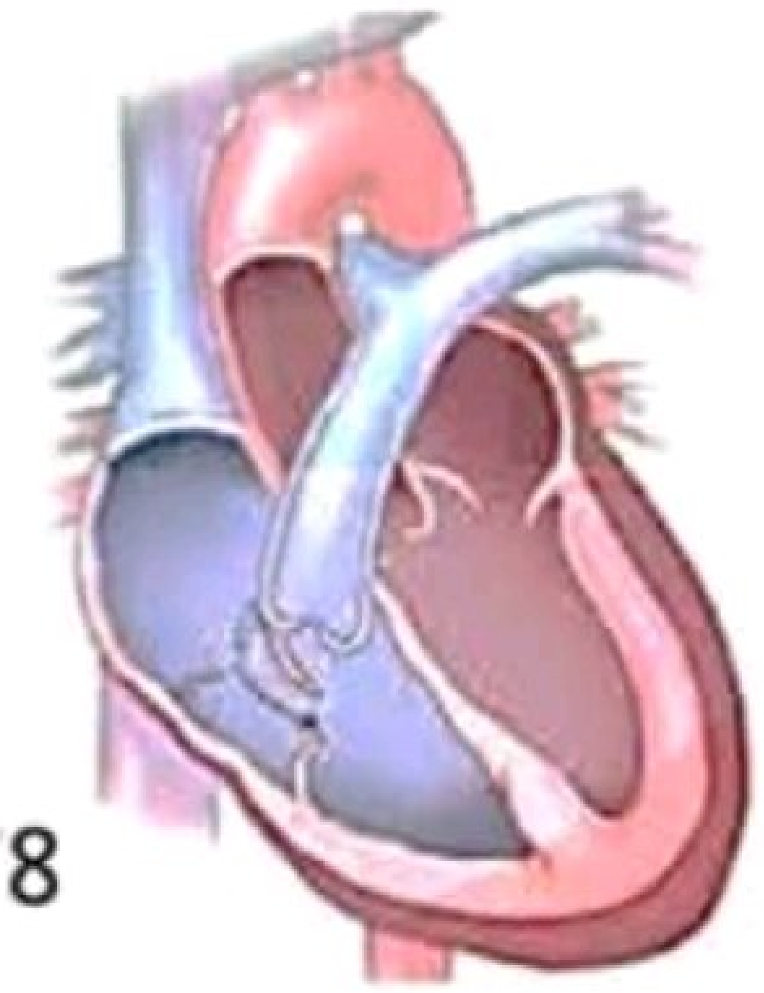
Lithium toxicity

Management
Hydration with NaCl
Mannitol diuresis
Amiloride

Adverse effects of lithium

- Leucocytosis
- Increase weight
- Tremor
- Hypothyoid Goitre
- Increase nausea, vomiting, diarrhea
- Urination: Nephrogenic diabetes inspidus
- Mental: ataxia, tinnitus, seizures
- Skin: Acneiform eruption

TERATOGENIC: EBSTEIN ANOMALY



- Tricuspid leaflets displaced inferiorly
- RV hypoplasia
- Tricuspid regurgitation or stenosis
- +/- patent foramen ovale

ANXIETY DISORDERS

Acute treatment- Benzodiazepine, overall to stabilize the patient- SSRI

1. GAD- Generalized Anxiety Disorder

- Free floating anxiety – always anxious
- Minimum 6 months duration required for diagnosis

2. Panic Disorder

- Feeling of impending doom
- In between period is absolutely normal
- Diagnosis of exclusion (after ruling out medical conditions- MI, Asthma)
- Situation Independent

3. Phobia

- Similar to panic disorder but with presence of a phobic stimuli
- Situation Dependent
- Types:
  - **AGORAPHOBIA-** Fear of Closed, Open & Crowded/Market places – difficult to escape situations. (All should be present)
  - **SOCIAL PHOBIA –** Fear of socially demanding situations (Stage Fear)
  - **Specific PHOBIA-** Fear of any one thing. Eg. Claustrophobia- Fear of only closed places.
- Rx: Systemic desensitization (Exposure therapy)

TRAUMA AND STRESS RELATED DISORDERS

1. PTSD

- >1-month duration required for diagnosis

2. Acute stress disorders

- < 1-month duration required for diagnosis

Both after a MAJOR life event
Triad of Hyperarousal,
Intrusiveness (Re-experience trauma),
Avoidance (Avoiding the conditions)
Rx: CBT- Cognitive Behavioural therapy

3. Adjustment Disorder

- After a mild to moderate routine live event
- Anxiety + Depression symptoms
- Rx: Supportive Psychotherapy (Teach the patient about coping skills)

Somatic Symptoms & related disorders

1. Somatisation disorder

- Multiple Symptoms (Pain, GI disturbance, Neurological)

2. Somatoform Pain disorder

- Only Pain symptom

3. Hypochondriasis

- AKA Illness Anxiety disorder
- Presents with a DIAGNOSIS

Conversion Disorders

- Hysteria- Pseudo-seizure
- AKA- Functional Neurological symptoms
- Has neurological symptoms without any organic problem
- Always after a stress factor

Dissociative Disorders

1. Dissociate Fugue- Patient travels, reaches to a new place, and assumes a new identity.
2. Identity Disorder- Multiple Personality disorder
3. Depersonalization and Derealisation disorder **[AS IF Phenomenon]**- There is transient feeling of detachment from self or environment as if the patient is observing himself from outside in. (Out of Self)
4. Dissociative Amnesia- Patchy loss of Autobiographical memory.

OCD & related Disorders

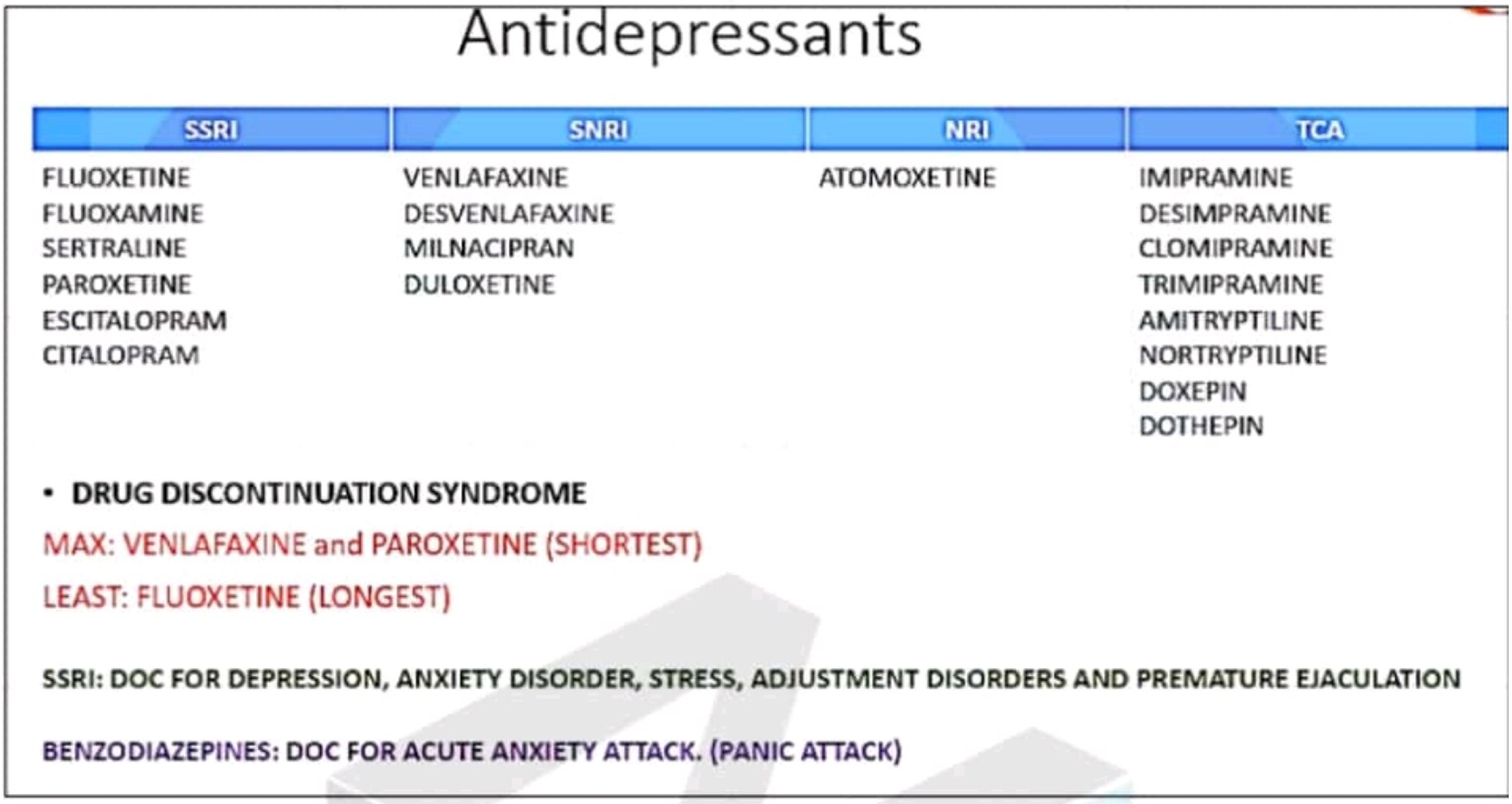
1. OCD – Obsessive Compulsive disorder

- Rx: DOC is SSRI, but Therapy of Choice is Exposure and Response prevention (ERP)

2. Body dysmorphic disorder

3. Others

  a) **Hoarding disorder**
  b) **Trichotillomania**
  c) **Excoriation disorder**



Antidepressants

SSRI	SNRI	NRI	TCA
FLUOXETINE	VENLAFAXINE	ATOMOXETINE	IMIPRAMINE
FLUOXAMINE	DESVENLAFAXINE		DESIMPRAMINE
SERTRALINE	MILNACIPRAN		CLOMIPRAMINE
PAROXETINE	DULOXETINE		TRIMIPRAMINE
ESCITALOPRAM			AMITRYPTILINE
CITALOPRAM			NORTRYPTILINE
			DOXEPIN
			DOTHEPIN

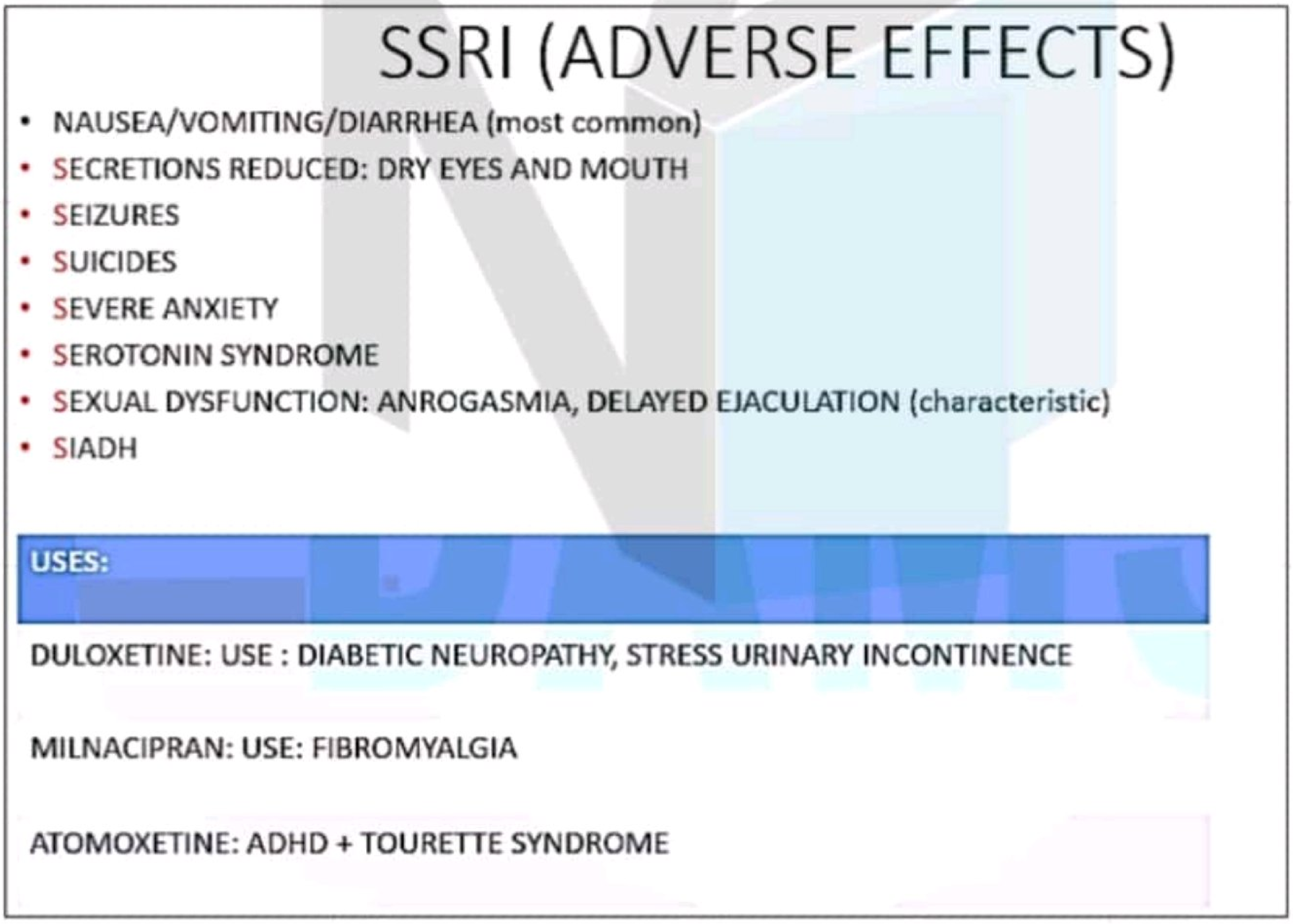
- **DRUG DISCONTINUATION SYNDROME**

MAX: VENLAFAXINE and PAROXETINE (SHORTEST)

LEAST: FLUOXETINE (LONGEST)

SSRI: DOC FOR DEPRESSION, ANXIETY DISORDER, STRESS, ADJUSTMENT DISORDERS AND PREMATURE EJACULATION

BENZODIAZEPINES: DOC FOR ACUTE ANXIETY ATTACK. (PANIC ATTACK)



SSRI (ADVERSE EFFECTS)

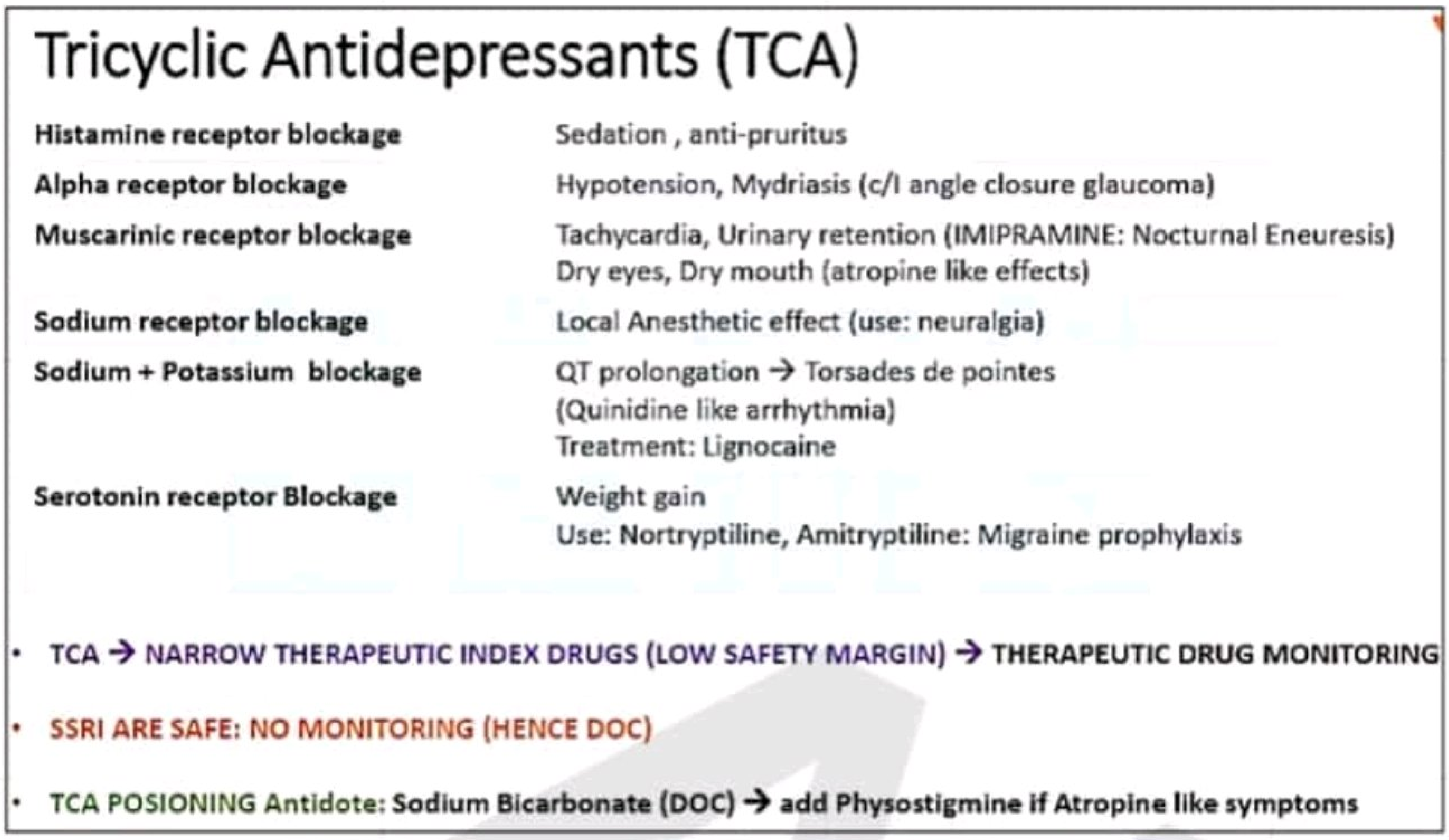
- NAUSEA/VOMITING/DIARRHEA (most common)
- SECRETIONS REDUCED: DRY EYES AND MOUTH
- SEIZURES
- SUICIDES
- SEVERE ANXIETY
- SEROTONIN SYNDROME
- SEXUAL DYSFUNCTION: ANROGASMIA, DELAYED EJACULATION (characteristic)
- SIADH

USES:

DULOXETINE: USE : DIABETIC NEUROPATHY, STRESS URINARY INCONTINENCE

MILNACIPRAN: USE: FIBROMYALGIA

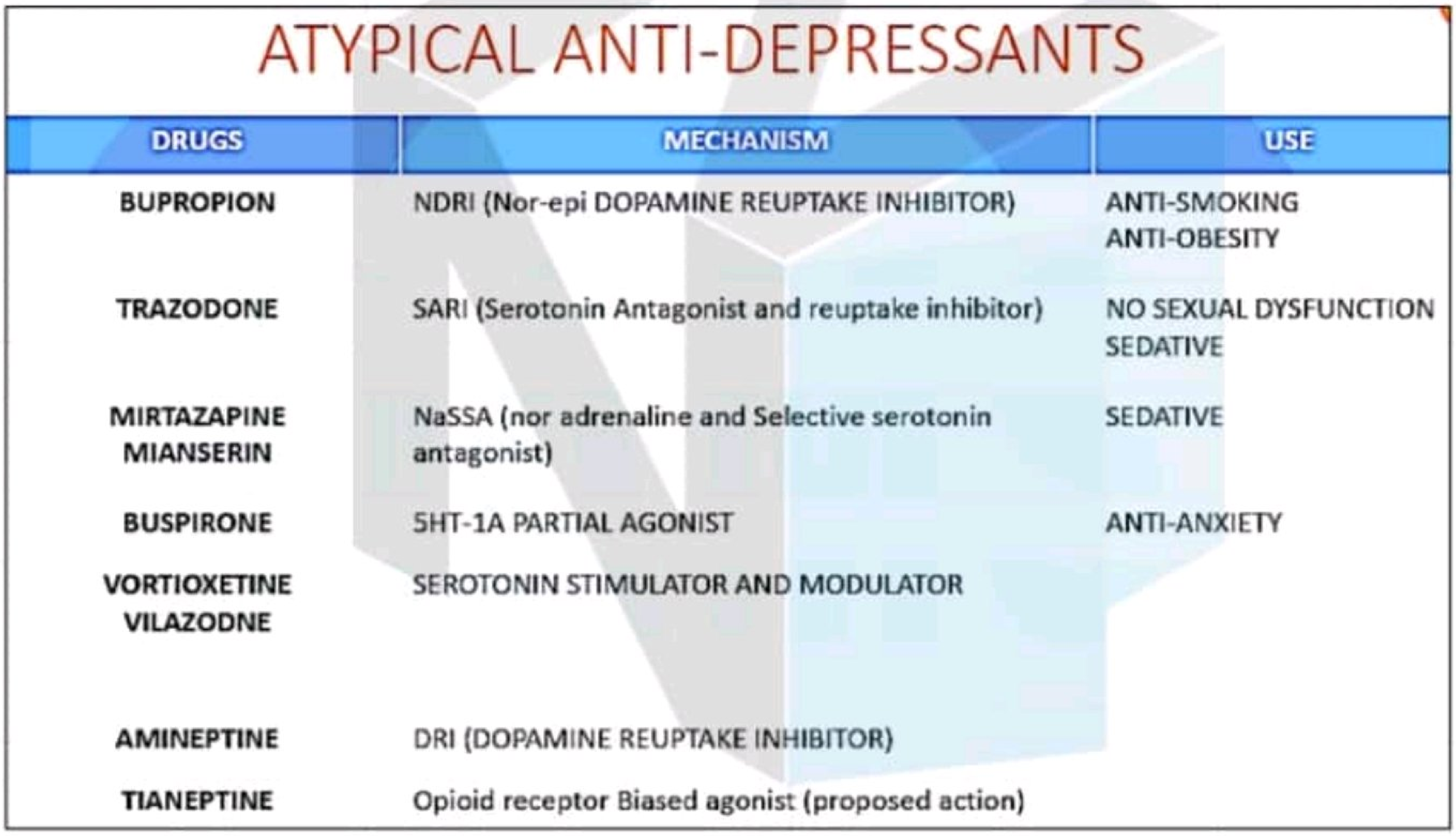
ATOMOXETINE: ADHD + TOURETTE SYNDROME



Tricyclic Antidepressants (TCA)

Histamine receptor blockage	Sedation , anti-pruritus
Alpha receptor blockage	Hypotension, Mydriasis (c/I angle closure glaucoma)
Muscarinic receptor blockage	Tachycardia, Urinary retention (IMIPRAMINE: Nocturnal Eneuresis) Dry eyes, Dry mouth (atropine like effects)
Sodium receptor blockage	Local Anesthetic effect (use: neuralgia)
Sodium + Potassium blockage	QT prolongation → Torsades de pointes (Quinidine like arrhythmia) Treatment: Lignocaine
Serotonin receptor Blockage	Weight gain Use: Nortryptiline, Amitryptiline: Migraine prophylaxis

- **TCA → NARROW THERAPEUTIC INDEX DRUGS (LOW SAFETY MARGIN) → THERAPEUTIC DRUG MONITORING**
- **SSRI ARE SAFE: NO MONITORING (HENCE DOC)**
- **TCA POSIONING Antidote: Sodium Bicarbonate (DOC) → add Physostigmine if Atropine like symptoms**



ATYPICAL ANTI-DEPRESSANTS

DRUGS	MECHANISM	USE
BUPROPION	NDRI (Nor-epi DOPAMINE REUPTAKE INHIBITOR)	ANTI-SMOKING ANTI-OBESITY
TRAZODONE	SARI (Serotonin Antagonist and reuptake inhibitor)	NO SEXUAL DYSFUNCTION SEDATIVE
MIRTAZAPINE **MIANSERIN**	NaSSA (nor adrenaline and Selective serotonin antagonist)	SEDATIVE
BUSPIRONE	5HT-1A PARTIAL AGONIST	ANTI-ANXIETY
VORTIOXETINE **VILAZODNE**	SEROTONIN STIMULATOR AND MODULATOR	
AMINEPTINE	DRI (DOPAMINE REUPTAKE INHIBITOR)	
TIANEPTINE	Opioid receptor Biased agonist (proposed action)	

- **Psychosis →** Antipsychotics
- **Mood disorder/Bipolar disorder →** Mood stabilizers
- **Unipolar depression →** Antidepressants
- **Bipolar depression →** Mood stabilizers + Antidepressants (alone will precipitate mania)
- **Neurosis/anxiety disorder:** Acute→ Benzodiazepines
  Maintenance → SSRI (Antidepressants)